**Efficacy of hypoglycemic treatment in type 2 diabetes stratified by age or diagnosed age: a meta-analysis**

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|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author , year** | **Study duration** | | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **SU versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Coniff, 1995[1](#_ENREF_1) | | 36 weeks | Acarbose | 67 | 56.2 | 39 | 29.7 | 5.1 | -0.54±1 | 6.88 | 81.6 | | -1.4±1 | |
| Tolbutamide | 66 | 55.4 | 56 | 29.5 | 5.6 | -0.93±1.0 | 6.95 | 84.8 | | +1.8±1 | |
| Placebo | 62 | 56.3 | 52 | 29.9 | 5.5 | 0.04±1.0 | 7.1 | 85.8 | | -1.4±1 | |
| Ebeling, 2001[2](#_ENREF_2) | | 6 months | Glibenclamide 2.5mg qd | 10 | 55.2 | / | 30.2±1.7 | 5.9 | -1.2±0.3 | 8.9±0.3 | / | | / | |
| Pioglitazone 30mg qd | 9 | 55.2 | / | 30.5±1.3 | 5.9 | -1.1±0.5 | 9.1±0.3 | / | | / | |
| PBO | 10 | 55.2 | / | 31.9±1.5 | 5.9 | -0.2±0.3 | 8.6±0.2 | / | | / | |
| Fischer, 2003[3](#_ENREF_3) | | 16 weeks | glibenclamide 1mg tid | 27 | 58.1±7.0 | 59.3 | / | 5.8±0.8 | -1.3±0.2 | 8.3±0.2 | 79.3±2.4 | | 1.6±2.4 | |
| acarbose 100mg tid | 25 | 59.4±5.6 | 76 | / | 7.8±0.9 | 0±0.3 | 8.1±0.2 | 78.2±2.3 | | -1.5±2.4 | |
| PBO | 25 | 58.6±6.3 | 68 | / | 6.4±0.9 | 0.7±0.3 | 8.3±0.2 | 79.2±1.8 | | -1.3±1.8 | |
| Goldberg, 1996[4](#_ENREF_4) | | 14 weeks | glimepiride 1mg Qd | 78 | 58.9 | 71.8 | / | 7 | 0.2±1 | 7.8 | 83.9 | | / | |
| glimepiride 4mg Qd | 76 | 57.8 | 53.9 | / | 5 | 0±1 | 7.7 | 86.1 | | / | |
| glimepiride 8mg Qd | 76 | 59.6 | 56.6 | / | 6 | -0.3±1 | 7.8 | 85.3 | | / | |
| PBO | 74 | 60.4 | 64.9 | / | 6 | 1.7±1 | 7.8 | 85.0 | | / | |
| Hanefeld, 2002[5](#_ENREF_5) | | 16 weeks | Acarbose | 11 | 60.4±1.3 | 91 | 27.5±0.7 | 7.7±1.3 | 0.4±0.6 | 8.2±0.3 | / | | / | |
| Glibenclamide 1mg tid | 8 | 60.6±2.5 | 62.5 | 27.1±1.1 | 7.1±1.2 | -0.8±0.6 | 8.4±0.4 | / | | / | |
| Placebo | 8 | 59±1.6 | 75 | 27.2±1.1 | 6.8±1.6 | 0.9±0.6 | 8.7±0.6 | / | | / | |
| Hoffmann, 1994[6](#_ENREF_6) | | 24 weeks | Glibenclamide 4.3mg qd | 27 | 59.5±5.7 | 48 | 26.5±2.1 | 1.4±1.1 | -0.8±0.37 | 8.30±0.37 | / | | / | |
| Acarbose 100mg tid | 28 | 58.8±6.9 | 46 | 26.5±1.6 | 1.0±0.9 | -0.99±0.42 | 8.29±0.42 | / | | / | |
| PBO | 30 | 56.9±6.7 | 40 | 26.8±1.5 | 1.0±0.9 | 0.11±0.37 | 8.29±0.37 | / | | / | |
| Madsbad, 2004[7](#_ENREF_7) | | 12 weeks | liraglutide 0.045mg Qd | 26 | 53±9.0 | 84.6 | 30.2±5.4 | 4.1±3.7 | 0.25±0.8 | 7.4±0.8 | / | | -0.03±0.96 | |
| liraglutide 0.225mg Qd | 24 | 58±7.5 | 62.5 | 32.0±5.3 | 4.4±4.0 | -0.34±0.8 | 7.9±0.8 | / | | -0.74±0.15 | |
| liraglutide 0.45mg Qd | 27 | 57±11.3 | 66.7 | 30.1±5.0 | 4.5±4.6 | -0.3±1 | 7.7±1.0 | / | | -1.2±0.02 | |
| liraglutide 0.60mg Qd | 30 | 57±7.7 | 66.7 | 30.4±4.8 | 4.6±4.6 | -0.7±1 | 7.4±1.2 | / | | 0.27±0.58 | |
| liraglutide 0.75mg Qd | 28 | 58±9.7 | 57.1 | 31.9±4.3 | 6.1±7.9 | -0.75±0.9 | 7.4±0.9 | / | | -0.39±0.44 | |
| PBO | 29 | 57±9.4 | 69 | 30.3±4.2 | 3.8±3.4 | -0.1±1.0 | 7.8±0.9 | / | | 0 | |
| Glimepiride 4mg qd | 26 | 57±9.2 | 61.5 | 30.2±4.6 | 3.4±2.9 | -0.74±1.2 | 7.4±1.2 | / | | 0.94±0.02 | |
| Rosenstock, 1996[8](#_ENREF_8) | | 14 weeks | glimepiride 8mg Qd | 88 | 61.8±9.9 | 74 | / | 7 | -0.7±1 | 8.1±1.0 | / | | / | |
| glimepiride 4mg bid | 81 | 58.8±10.2 | 70 | / | 6 | / | 8.1±1.2 | / | | / | |
| glimepiride 16mg Qd | 83 | 59.6±9.9 | 66 | / | 5 | / | 8.0±1.2 | / | | / | |
| glimepiride 8mg bid | 85 | 61.7±8.9 | 72 | / | 7 | / | 8.3±1.2 | / | | / | |
| PBO | 79 | 61.1±9.7 | 67 | / | 6 | 1.7±1.1 | 8.0±1.1 | / | | / | |
| Segal, 1997[9](#_ENREF_9) | | 24 weeks | Miglitol 100mg tid | 40 | 61 | 55 | 28.6 | / | -0.60±1 | 7.95 | / | | -1.4±1 | |
| Glibenclamide 3.5mg bid | 37 | 56 | 62.2 | 29.2 | / | -0.86±1 | 7.96 | / | | +1.4±1 | |
| PBO | 42 | 59 | 57.1 | 29.1 | / | 0.15±1 | 8.25 | / | | 0±1 | |
| Scott, 2007[10](#_ENREF_10) | | 12 weeks | Sitagliptin 5mg bid | 125 | 55.1±9.5 | 49.6 | 30.8±5.1 | 4.3±4.1 | -0.15±0.14 | 7.9±1.0 | / | | 0.1±1 | |
| Sitagliptin 12.5mg bid | 123 | 56.2±9.0 | 48 | 30.5±5.0 | 4.9±5.0 | -0.41±0.14 | 7.9±0.9 | / | | 0.1±1 | |
| Sitagliptin 25mg bid | 123 | 55.6±9.0 | 57.7 | 31.4±6.9 | 5.0±5.2 | -0.43±0.13 | 7.9±0.9 | / | | 0.3±1 | |
| Sitagliptin 50mg bid | 124 | 55.1±9.8 | 52.4 | 30.4±4.9 | 4.2±4.0 | -0.54±0.14 | 7.8±1.0 | / | | 0.4±1 | |
| placebo | 125 | 55.3±9.7 | 62.4 | 31.6±5.8 | 4.7±4.2 | 0.23±0.135 | 7.9±1.0 | / | | 0±1 | |
| Glipizide 20mg qd | 123 | 54.7±10.7 | 56.9 | 30.6±5.3 | 4.7±4.2 | -0.76±0.16 | 7.9±1 | / | | +0.9±1 | |
| Simonson, 1997[11](#_ENREF_11) | | 16 weeks | glipizide 5mg | 68 | 57.4 | 58.8 | 29 | 6.9 | -0.9±0.2 | 8.5±0.2 | 83.9 | | -0.14±0.18 | |
| glipizide 10mg | 42 | 58.7 | 59.5 | 28.4 | 8.8 | -1.2±0.2 | 8.8±0.2 | 82.1 | | / | |
| glipizide 15mg | 42 | 55.5 | 61.9 | 29.5 | 6.5 | -0.49±0.2 | 8.6±0.2 | 84.8 | | / | |
| glipizide 20mg | 69 | 59.3 | 68.1 | 28.8 | 7.8 | -0.9±0.2 | 8.7±0.2 | 84.8 | | / | |
| glipizide 40mg | 28 | 61.7 | 60.7 | 29.6 | 6.6 | -1.27±0.3 | 8.4±0.3 | 88.9 | | / | |
| glipizide 60mg | 29 | 56.9 | 79.3 | 30.5 | 5.3 | -1.1±0.3 | 8.6±0.3 | 91.2 | | / | |
| PBO | 69 | 60.2 | 76.8 | 29.7 | 7.5 | 0.84±0.2 | 8.3±0.2 | 87.1 | | -3.1±0.4 | |
| **SU versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Burant, 2012[12](#_ENREF_12) | | 12 weeks | TAK-875 6.25mg Qd | 60 | 51.6±10.4 | 48 | 32.2±5.3 | 5.7±5.2 | -0.65±1.0 | 8.60±0.96 | 85.8±18.4 | | / | |
| TAK-875 25mg Qd | 61 | 51.3±10.9 | 46 | 32.3±4.6 | 5.2±4.6 | / | 8.23±0.93 | 88.4±22.7 | | / | |
| TAK-875 50mg Qd | 60 | 52.1±10.8 | 47 | 31.0±4.6 | 6.2±5.4 | -1.12±0.8 | 8.33±0.80 | 83.7±16.3 | | / | |
| TAK-875 100mg Qd | 62 | 51.8±10.1 | 47 | 32.3±5.4 | 4.8±3.8 | -1.0±0.9 | 8.33±0.87 | 88.9±22.5 | | / | |
| TAK-875 200mg Qd | 60 | 49.0±10.7 | 48 | 31.3±4.8 | 6.4±5.0 | / | 8.56±0.93 | 84.6±18.3 | | / | |
| glimepiride 4mg Qd | 62 | 52.2±9.7 | 55 | 31.0±5.4 | 6.4±5.7 | -1.05±0.8 | 8.43±0.81 | 83.5±17.8 | | +0.86±17.8 | |
| PBO | 61 | 52.9±11.3 | 43 | 31.2±5.0 | 5.6±4.8 | -0.13±1.0 | 8.46±1.07 | 84.5±20.7 | | -0.73±20.7 | |
| Camerini-Davalos, 1994[13](#_ENREF_13) | | 3 years | Glipizide 5mg qd+insulin | 40 | 45.2±1.7 | / | 25.1±0.2 | 10.5 | -1.6±0.3 | 11.2±0.3 | / | | / | |
| PBO+insulin | 29 | 46.4±2.0 | / | 24.3±0.4 | 14.1 | 0.2±0.4 | 10.3±0.3 | / | | / | |
| Feinglos, 2005[14](#_ENREF_14) | | 16 weeks | glipizide 2.5mg/day+met | 61 | 57.7±10.7 | 45.9 | 31.7±4.4 | 6.5 | -0.66±0.1 | 7.45 | 90±18.7 | | +0.4±18.7 | |
| PBO+met | 61 | 58.8±10.0 | 41 | 32.1±4.9 | 4.6 | -0.19±0.1 | 7.64 | 90.8±18.4 | | -1.7±18.4 | |
| Forst, 2010[15](#_ENREF_15) | | 12 weeks | Linagliptin 1mg+met | 65 | 59.1±8.4 | 55.4 | 32.2±4.3 | 6.9±5.9 | -0.15±0.7 | 8.2±0.7 | 92.5±16.9 | | -0.15±16.9 | |
| Linagliptin 5mg+met | 66 | 59.6±9.8 | 56.1 | 31.7±4.5 | 7.3±7.5 | -0.5±0.81 | 8.5±0.8 | 90.7±14.2 | | -0.57±14.2 | |
| Linagliptin 10mg+met | 66 | 61.8±8.8 | 53 | 31.7±4.5 | 8.2±6.8 | -0.42±0.7 | 8.4±0.7 | 89.9±16.3 | | -1.27±16.3 | |
| Glimepiride 3mg qd | 65 | 59.4±9.9 | 63.1 | 31.5±4.2 | 6.7±5.9 | -0.68±0.7 | 8.2±0.7 | 90.5±15 | | +0.73±15 | |
| Placebo+met | 71 | 60.1±8.1 | 62 | 32.2±4.2 | 6.2±5.1 | 0.25±0.7 | 8.4±0.7 | 93.1±16.8 | | -0.84±16.8 | |
| Karlander, 1991[16](#_ENREF_16) | | 325 days | Glyburide 10.5mg qd+insulin | 10 | 57.1 | / | / | 14.1 | -2.0±1.5 | 11.1±1.5 | 83.5±18.5 | | 6.1±18.5 | |
| placebo+insulin | 10 | 57.1 | / | / | 14.1 | -1.3±2.5 | 10.3±2.5 | 82.7±26.0 | | 3.4±26.0 | |
| Lewitt, 1989[17](#_ENREF_17) | | 6 months | glyburide15mg/day+insulin | 31 | / | / | 26.7±2.9 | / | -0.8±1.3 | 9.9±1.3 | / | | / | |
| PBO+insulin | / | / | / | 0.4±1.3 | / | | / | |
| Lins, 1988[18](#_ENREF_18) | | 12 weeks | Glibenclamide 3.5mg bid +insulin | 10 | 67±2 | 40 | / | / | -1.2±0.8 | 8.2±0.8 | / | | / | |
| PBO+insulin | 10 | 60±3 | 60 | / | / | 0.3±0.5 | 8.1±0.5 | / | | / | |
| Nauck, 2009[19](#_ENREF_19) | | 26 weeks | liraglutide 0.6mg/day+met | 242 | 56±11 | 62 | 30.5±4.8 | 7±5 | -0.7±0.1 | 8.4±0.9 | / | | -1.8±0.2 | |
| liraglutide 1.2mg/day+met | 240 | 57±9 | 54 | 31.1±4.8 | 7±5 | -1.0±0.1 | 8.3±1.0 | / | | -2.6±0.2 | |
| liraglutide 1.8mg/day+met | 242 | 57±9 | 59 | 30.9±4.6 | 8±5 | -1.0±0.1 | 8.4±1.0 | / | | -2.8±0.2 | |
| glimepiride 4mg/day+met | 242 | 57±9 | 57 | 31.2±4.6 | 8±5 | -1±0.1 | 8.4±1.0 | / | | +1.0±0.2 | |
| PBO+met | 121 | 56±9 | 60 | 31.6±4.4 | 8±6 | 0.1±0.1 | 8.4±1.1 | / | | -1.5±0.3 | |
| Riddle, 1992[20](#_ENREF_20) | | 16 weeks | glyburide 20mg/day+insulin | 11 | / | / | / | / | -1.3±0.1 | 11.0±0.1 | / | | +4.9±1.0 | |
| PBO+insulin | 10 | / | / | / | / | -0.8±0.2 | 10.9±0.2 | / | | +3.3±0.2 | |
| Riddle, 1998[21](#_ENREF_21) | | 24 weeks | Glimepiride 8mg bid+insulin | 72 | 58±8 | 62.5 | 32.2±4.4 | 7±4 | -2.1±1.2 | 9.7±1.3 | 93.9±15.9 | | +4.3±16.5 | |
| PBO+insulin | 73 | 58±8 | 54.8 | 33.7±5.4 | 7±4 | -2.1±1.2 | 9.8±1.3 | 99.2±20.8 | | +4.0±20.8 | |
| Roberts, 2005[22](#_ENREF_22) | | 26 weeks | Glimepiride 8mg qd+metformin+SU | 82 | 56.5±9.8 | 61 | 33.98±5.15 | 8.7±6.8 | -1.31±0.08 | 8.15±0.76 | 100.88±18.97 | | +3.76±0.54 | |
| PBO+metformin+SU | 77 | 56.4±10.0 | 62.3 | 32.76±5.11 | 7.9±4.9 | -0.33±0.08 | 8.15±0.65 | 96.31±19.1 | | +0.45±0.52 | |
| Schade, 1987[23](#_ENREF_23) | | 4 months | Glyburide 20mg qd+insulin | 8 | / | / | / | / | -0.4±0.5 | 10.6±0.4 | 84.6±4.4 | | / | |
| PBO+insulin | 8 | / | / | / | / | 0.3±0.4 |  | |
| Stuart, 1997[24](#_ENREF_24) | | 12 weeks | Glyburide 3mg bid+insulin | 9 | / | / | / | / | -0.3±0.3 | 7.7±0.2 | 98±3.2 | | 0±4.7 | |
| PBO+insulin | 9 | / | / | / | / | 0.1±0.3 | 7.4±0.3 | 98±3.2 | | -1±4.4 | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **MET versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Chiasson, 2001[25](#_ENREF_25) | | 36 weeks | Miglitol 100mg tid | 82 | 57.3±9.0 | 78.1 | 31.1±4.5 | 5.2±4.7 | 0.02±0.10 | 8.2±0.9 | 91±15.5 | | -0.42±0.29 | |
|  | |  | Metformin 500mg tid | 83 | 57.9±8.6 | 73.5 | 30.7±5.1 | 7.5±7.4 | -0.85±0.12 | 8.2±0.9 | 89±17.8 | | -0.79±0.33 | |
| miglitol+metformin | 76 | 58.9±7.9 | 77.6 | 29.5±3.8 | 6.1±5.5 | -1.39±0.11 | 8.3±0.8 | / | | / | |
|  | |  | placebo | 83 | 57.7±9.9 | 67.5 | 31.1±4.4 | 5.1±4.9 | 0.38±0.12 | 8.1±0.7 | 88.6±14.1 | | -0.69±0.27 | |
| DeFronzo, 1995[26](#_ENREF_26) | | 29weeks | Metformin 2550mg qd | 143 | 53±1 | 43.4 | 29.9±0.3 | 6.0±0.5 | -1.4±0.1 | 8.4±0.1 | 94.4±1.1 | | -0.6±0.3 | |
| placebo | 146 | 53±1 | 42.5 | 29.2±0.3 | 6.0±0.6 | 0.4±0.1 | 8.2±0.2 | 92.2±1.2 | | -1.1±1.2 | |
| Dornan, 1991[27](#_ENREF_27) | | 8 months | Metformin 1g tid | 30 | 55±1 | / | 30±1 | / | -1.4±0.4 | 11.7±0.4 | 84.6±2.7 | | 0±2.7 | |
| placebo | 30 | 55±1 | / | 30±1 | / | 1.5±0.4 | 11.8±0.4 | 79.5±2.5 | | -0.9±2.5 | |
| Fonseca, 2013[28](#_ENREF_28) | | 12 weeks | ipraliflozin 12.5mg Qd | 70 | 53.9±9.6 | 55.7 | 31.0±5.9 | 4.08±3.24 | -0.22±0.8 | 7.95±0.78 | 86±22.3 | | -1.5±0.75 | |
| ipraliflozin 50mg Qd | 67 | 52.6±10.7 | 50.7 | 32.2±5.9 | 4.61±4.65 | -0.39±0.8 | 8.05±0.81 | 90.7±20.8 | | -1.66±7.5 | |
| ipraliflozin 150mg Qd | 68 | 54.2±10.3 | 42.6 | 30.9±6.3 | 5.11±6.46 | -0.47±0.6 | 7.83±0.65 | 83.3±21.6 | | -2.08±7.5 | |
| ipraliflozin 300mg Qd | 68 | 54.2±10.7 | 54.4 | 30.7±5.0 | 4.48±4.91 | -0.55±0.6 | 7.90±0.67 | 86.7±19.6 | | -2.67±7.5 | |
| Metformin 1500mg qd | 69 | 53.1±11.7 | 58 | 29.8±5.5 | 4.13±4.71 | -0.46±0.9 | 8.03±0.90 | 84.1±21.8 | | -0.88±7.5 | |
| PBO | 69 | 53.4±9.7 | 46.4 | 30.9±5.5 | 4.64±5.93 | 0.26±0.78 | 7.84±0.78 | 81.8±17.4 | | -1±7.5 | |
| Fujioka, 2005[29](#_ENREF_29) | | 24 weeks | metformin 1000mg once daily | 161 | 55±11 | 53 | 28.7±3.9 | 3.3±2.8 | -0.6±0.9 | 8.1±0.9 | / | | / | |
| placebo | 79 | 58±11 | 63 | 28.9±3.5 | 3.2±2.6 | 0.2±0.9 | 7.9±0.9 | / | | / | |
| 16 weeks | metformin 500mg once daily | 128 | 55±11 | 44 | 30.1±4.0 | 3.3±2.9 | -0.5±0.9 | 8.2±0.9 | / | | / | |
| metformin 1000mg once daily | 120 | 56±10 | 58 | 30.6±4.2 | 3.0±2.7 | -0.6±1.1 | 8.4±1.1 | / | | / | |
| metformin 1500mg once daily | 120 | 56±11 | 48 | 29.7±4.0 | 2.9±2.7 | -0.9±2.6 | 9.9±2.6 | / | | / | |
| metformin 2000mg once daily | 134 | 55±11 | 41 | 30.9±4.0 | 2.7±2.5 | -0.9±1.1 | 8.4±1.1 | / | | / | |
| metformin 1000mg twice daily | 123 | 57±10 | 47 | 30.6±4.6 | 3.1±2.7 | -1.1±1.1 | 8.4±1.1 | / | | / | |
| placebo | 117 | 54±10 | 49 | 30.7±4.1 | 2.7±2.7 | 0.1±1.1 | 8.3±1.1 | / | | / | |
| Garber, 1997[30](#_ENREF_30) | | 14 weeks | metformin 500mg daily | 73 | 57±10 | 62 | / | / | 0.3±1.7 | 10.1±1.7 | 90±20.3 | | / | |
| metformin 1000mg daily | 73 | 55±10 | 55 | / | / | 0.01±2.0 | 10.0±2.0 | 90±18.9 | | / | |
| metformin 1500mg daily | 76 | 59±10 | 63 | / | / | -0.5±1.5 | 9.7±1.5 | 89.6±16.2 | | / | |
| metformin 2000mg daily | 73 | 60±11 | 53 | / | / | -0.8±2.1 | 10.1±2.1 | 89.1±20.3 | | / | |
| metformin 2500mg daily | 77 | 59±11 | 65 | / | / | -0.4±1.8 | 10.0±1.8 | 94.5±23.4 | | / | |
| placebo | 79 | 55±11 | 56 | / | / | 1.2±1.9 | 9.9±1.9 | 90.9±20.1 | | / | |
| Goldstein, 2007[31](#_ENREF_31) | | 24 weeks | Sitagliptin | 175 | 53.3±10.2 | 52.0 | 31.2±5.9 | 4.4±4.6 | -0.66±0.165 | 8.87±0.99 | / | | / | |
| Metformin 500mg bid | 178 | 53.4±10.2 | 48.9 | 32.1±6.8 | 4.5±3.9 | -0.82±0.16 | 8.90±1.00 | / | | / | |
| Metformin 1000mg bid | 177 | 53.2±9.6 | 45.1 | 32.2±7.1 | 4.4±4.4 | -1.13±0.16 | 8.68±0.91 | / | | / | |
| placebo | 165 | 53.6±10.0 | 52.8 | 32.5±6.7 | 4.6±4.9 | 0.17±0.165 | 8.68±1.00 | / | | / | |
| Hällsten, 2002[32](#_ENREF_32) | | 26 weeks | metformin 1g bid | 13 | 57.8±2.2 | 61.5 | 29.9±1.1 | / | -0.7±0.2 | 6.9±0.2 | / | | / | |
| rosiglitazone 4mg bid | 14 | 58.6±2.0 | 71.4 | 29.3±1.0 | / | -0.3±0.2 | 6.8±0.2 | / | | / | |
| placebo | 14 | 57.7±1.9 | 71.4 | 30.3±1.2 | / | -0.2±0.1 | 6.3±0.1 | / | | / | |
| Haak, 2012[33](#_ENREF_33) | | 24 weeks | Linagliptin 5 mg | 142 | 56.2±10.8 | 56.3 | 29.0±4.7 | / | -0.5±0.1 | 8.7±1.0 | 79.1±17.3 | | / | |
| Metformin 500mg bid | 141 | 52.9±10.4 | 56.9 | 28.9±4.8 | / | -0.6±0.1 | 8.7±0.9 | 79.9±18.4 | | / | |
| Metformin 1000mg bid | 138 | 55.2±10.6 | 53.1 | 29.5±5.3 | / | -1.1±0.1 | 8.5±0.9 | 80±18.5 | | / | |
| Placebo | 72 | 55.7±11.0 | 50 | 28.6±5.2 | / | 0.1±0.1 | 8.7±1.0 | 76.8±17.5 | | / | |
| Hoffmann, 1997[34](#_ENREF_34) | | 24 weeks | Acarbose | 31 | 58.9±9.4 | 19 | 26.4±2.7 | 3.0±2.3 | -1.1±0.9 | 9.6±0.9 | 73.9±10.3 | | -0.8±10.3 | |
| Metformin | 31 | 55.9±7.8 | 45 | 27.4±2.2 | 2.1±1.5 | -1.0±0.9 | 9.7±0.9 | 79±8.8 | | +0.2±8.8 | |
| Placebo | 32 | 60.2±8.6 | 38 | 26.3±2.2 | 3.6±2.8 | 0.4±0.9 | 9.4±0.9 | 74.9±9.7 | | -0.5±9.7 | |
| Horton, 2000[35](#_ENREF_35) | | 24 weeks | metformin 500mg tid | 178 | 56.8±10.9 | 68.5 | 29.6±4.3 | 4.5±5.5 | -0.8±1.1 | 8.4±1.2 | / | | / | |
| nateglinide 120mg tid | 179 | 58.6±10.7 | 61.5 | 29.6±3.8 | 4.7±5.5 | -0.5±1.0 | 8.3±1.0 | / | | / | |
| nateglinide+metformin | 172 | 58.4±10.9 | 58.7 | 30.0±3.7 | 4.5±5.3 | -1.4±1 | 8.4±1.1 | / | | / | |
| placebo | 172 | 59.6±10.9 | 60.5 | 29.2±3.9 | 4.6±4.7 | 0.5±1.1 | 8.3±1.1 | / | | / | |
| List, 2009[36](#_ENREF_36) | | 12 weeks | dapagliflozin 2.5mg | 59 | 55±11 | 49 | 32±5 | / | -0.71±0.09 | 7.6±0.7 | 90±20 | | -2.7±0.75 | |
| dapagliflozin 5mg | 58 | 55±12 | 48 | 32±5 | / | -0.72±0.09 | 8.0±0.9 | 89±7 | | -2.5±0.75 | |
| dapagliflozin 10mg | 47 | 54±9 | 53 | 31±5 | / | -0.85±0.11 | 8.0±0.8 | 86±17 | | -2.7±0.85 | |
| dapagliflozin 20mg | 59 | 55±10 | 54 | 31±5 | / | -0.55±0.09 | 7.7±0.9 | 88±18 | | -3.4±0.75 | |
| dapagliflozin 50mg | 56 | 53±10 | 45 | 32±4 | / | -0.9±0.1 | 7.8±1.0 | 92±19 | | -3.4±0.75 | |
| PBO | 54 | 53±11 | 56 | 32±5 | / | -0.18±0.1 | 7.9±0.9 | 89±18 | | -1.2±0.75 | |
| Metformin 1500mg qd | 56 | 54±9 | 48 | 32±5 | / | -0.73±0.1 | 7.6±0.8 | 88±20 | | -1.7±0.75 | |
| Natali, 2004[37](#_ENREF_37) | | 16 weeks | Metformin 1500mg qd | 28 | 58±10 | 78.6 | 28.0±3.5 | 6.3±5.3 | -0.33±1.1 | 7.8±1.1 | 77.3±12.5 | | -0.6±0.4 | |
| rosiglitazone | 24 | 59±7 | 91.7 | 27.6±2.8 | 6.5±4.5 | 0.09±1.2 | 7.2±1.2 | 80.4±10.1 | | 0.5±0.5 | |
| PBO | 22 | 58±9 | 81.8 | 30.2±3.1 | 3.4±3.4 | 1.3±0.8 | 7.6±0.8 | 86.9±10.5 | | -0.3±0.8 | |
| Tessari, 1994[38](#_ENREF_38) | | 4 weeks | Metformin 850mg bid | 11 | 53±3 | 54.5 | 28±1 | / | -0.1±0.8 | 8.0±0.6 | / | | / | |
| placebo | 6 | 60±3 | 33.3 | 28±1 | / | -0.1±0.5 | 6.7±0.3 | / | | / | |
| Viljanen, 2005[39](#_ENREF_39) | | 26 weeks | Rosiglitazone 4mg bid | 14 | 58.6±7.7 | 64.3 | 29.3±4.0 | / | -0.3±0.9 | 6.8±0.9 | 83.7±8.1 | | +0.6±9.2 | |
| Metformin 1g bid | 12 | 57.8±8.7 | 58.3 | 29.6±4.0 | / | -0.6±0.9 | 6.9±0.9 | 87.6±10.7 | | -1.8±10.7 | |
| PBO | 11 | 58.7±8.3 | 81.8 | 29.8±4.1 | / | -0.1±0.7 | 6.2±0.7 | 89.1±9.3 | | +0.4±9.4 | |
| **MET versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Avilés-Santa, 1999[40](#_ENREF_40) | | 24 weeks | Metformin 2500mg qd+insulin | 21 | 53.1±9.4 | 28.6 | / | 9.2±6.4 | -0.23±1.4 | 9.0±1.4 | 103.9±25.2 | | +0.5±2.4 | |
| Placebo+insulin | 22 | 54.6±7.8 | 45.5 | / | 10.1±4.7 | -0.15±1.5 | 9.1±1.5 | 106.6±23.2 | | +3.2±2 | |
| Chiasson, 2001[25](#_ENREF_25) | | 36 weeks | Miglitol 100mg tid | 82 | 57.3±9.0 | 78.1 | 31.1±4.5 | 5.2±4.7 | 0.02±0.10 | 8.2±0.9 | 91±15.5 | | -0.42±0.29 | |
| Metformin 500mg tid | 83 | 57.9±8.6 | 73.5 | 30.7±5.1 | 7.5±7.4 | -0.85±0.12 | 8.2±0.9 | 89±17.8 | | -0.79±0.33 | |
| miglitol+metformin | 76 | 58.9±7.9 | 77.6 | 29.5±3.8 | 6.1±5.5 | -1.39±0.11 | 8.3±0.8 | / | | / | |
| placebo | 83 | 57.7±9.9 | 67.5 | 31.1±4.4 | 5.1±4.9 | 0.38±0.12 | 8.1±0.7 | 88.6±14.1 | | -0.69±0.27 | |
| Douek, 2005[41](#_ENREF_41) | | 12 months | Metformin 2g qd+insulin | 92 | 58±8.9 | 67.4 | 30.9±4.5 | 9±5.2 | -1.5±1.4 | 9.7±1.3 | 88.5±14.7 | | 6.3±14.7 | |
| Placebo+insulin | 91 | 58±7.7 | 62.6 | 31.5±4.3 | 10±5.2 | -1.3±1.5 | 10.0±1.5 | 91.1±15.7 | | 7.5±15.7 | |
| Gram, 2011[42](#_ENREF_42) | | 2 years | PBO+NPH | 46 | 55.8±7.7 | 71.7 | 34.0±6.0 | 7.3±4.3 | -0.4±1.4 | 8.7±1.3 | 100.2±19.8 | | +5.3±20 | |
| Metformin 1000mg bid+NPH | 45 | 55.4±8.5 | 57.8 | 35.7±6.4 | 8.2±4.0 | -1.3±1.3 | 8.9±1.2 | 105.1±17.7 | | 2.9±20 | |
| Rosiglitazone 4mg bid+NPH | 46 | 57.3±8.9 | 60.9 | 34.0±5.7 | 9.2±6.9 | -0.8±1.6 | 8.7±1.2 | 100.9±16.5 | | 7.6±20 | |
| metformin+rosiglitazone  +NPH | 46 | 57.3±8.2 | 65.2 | 34.4±7.0 | 8.1±5.3 | -1.7±1.1 | 8.5±1.1 | / | | / | |
| PBO+ASP | 48 | 57.1±8.5 | 47.9 | 33.7±5.0 | 9.1±5.5 | -0.6±1.2 | 8.5±1.2 | 98.3±16.6 | | 6.1±19 | |
| Metformin 1000mg bid+ASP | 45 | 56.1±8.2 | 62.2 | 33.7±6.1 | 8.7±4.5 | -1.2±1.2 | 8.5±1.2 | 100.5±17.9 | | 3.9±20 | |
| Rosiglitazone 4mg bid+ASP | 47 | 56.1±8.3 | 57.4 | 32.7±4.7 | 9.4±6.3 | -1.2±1 | 8.3±1.0 | 95.6±14.6 | | 10.4±20 | |
| metformin+rosiglitazone  +ASP | 48 | 55.3±9.1 | 70.8 | 32.9±4.4 | 9.0±5.8 | -1.5±1.2 | 8.5±1.2 | / | | / | |
| Hermann, 2001[43](#_ENREF_43) | | 12 months | metformin 850mg bid+insulin | 16 | 56.9±10.2 | 43.8 | 33.6±3.5 | 13 | -1.1±1.3 | 9.1±1.3 | 96.4±16.5 | | -1.4±16.5 | |
| Placebo+insulin | 19 | 58.1±9.7 | 63.2 | 32.6±3.8 | 13 | 0.3±1.0 | 8.7±1.0 | 94.2±9.4 | | +0.2±9.4 | |
| Kooy, 2009[44](#_ENREF_44) | | 4.3 years | metformin 850mg tid hydrochloride+insulin | 196 | 64±10 | 41.3 | 30±5 | 14±9 | -0.2±1.1 | 7.9±1.2 | 85±16 | | +2±17 | |
| placebo+insulin | 194 | 59±11 | 50 | 30±5 | 12±8 | 0.0±1.1 | 7.9±1.2 | 87±15 | | +4±17 | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **AGI versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Chan, 1998[45](#_ENREF_45) | | 24 weeks | Acarbose 100mg tid | 63 | 52.8 (10.2) | 50.8 | / | 2.7±3.5 | -0.7±0.3 | 8.2±1.0 | 64.1±10 | | -1.31±1.1 | |
| Placebo | 63 | 54 (10) | 50.8 | / | 2.1±3.4 | -0.27±0.27 | 8.6±1.1 | 65.4±13.3 | | 0.16±1.0 | |
| Chiasson, 1994[46](#_ENREF_46) | | 1 year | Acarbose 200mg qd | 38 | / | / | 28.8±0.5 | / | -0.9±0.2 | 6.7±0.2 | 84.5±1.2 | | -0.3±1.6 | |
| Placebo | 39 | / | / | 28.8±0.5 | / | 0±0.2 | 81.3±1.2 | | +0.1±1.3 | |
| Chiasson, 2001[25](#_ENREF_25) | | 36 weeks | Placebo | 83 | 57.7±9.9 | 67.5 | 31.1±4.5 | 5.1±4.9 | -0.235±0.06 | 8.1±0.7 | 91±15.5 | | -0.42±0.29 | |
| Miglitol | 82 | 57.3±9 | 78 | 31.1±4.4 | 5.2±4.7 | -0.685±0.05 | 8.2±0.9 | 88.6±14.1 | | -0.69±0.27 | |
| Coniff, 1994[47](#_ENREF_47) | | 36 weeks | Acarbose 50-300mg tid | 91 | 56.0±1.0 | 54 | 32 | 4 | -0.06±1 | 6.78 | 93.4±1.8 | | -0.93±1.8 | |
| Placebo | 98 | 55.6±1.0 | 45 | 31.5 | 3 | 0.53±1.0 | 6.65 | 94.5±1.7 | | -0.77±1.7 | |
| Coniff, 1995[48](#_ENREF_48) | | 16 weeks | Acarbose 100mg tid | 58 | 55 | 53 | 31 | 6 | -0.45±1 | 8.69 | 85.9 | | -0.19±1 | |
| Acarbose 200mg tid | 54 | 56 | 59 | 31 | 5 | -0.4±1 | 8.96 | 87.9 | | -0.8±1 | |
| Acarbose 300mg tid | 53 | 54 | 58 | 30 | 5 | -0.77±1 | 9.54 | 84.5 | | -0.45±1 | |
| Placebo | 64 | 54 | 58 | 32 | 5 | 0.33±1.0 | 8.67 | 91.3 | | -0.37±1 | |
| Coniff, 1995[1](#_ENREF_1) | | 36 weeks | Acarbose 200mg tid | 67 | 56.2 | 39 | 29.7 | 5.1 | -0.54±1 | 6.88 | 81.6 | | -1.4±1 | |
| Tolbutamide 250-1000mg tid | 66 | 55.4 | 56 | 29.5 | 5.6 | -0.93±1.0 | 6.95 | 84.8 | | +1.8±1 | |
| Placebo | 62 | 56.3 | 52 | 29.9 | 5.5 | 0.04±1.0 | 7.1 | 85.8 | | -1.4±1 | |
| Fischer, 2003[3](#_ENREF_3) | | 16 weeks | Acarbose 100mg tid | 25 | 59.4±5.6 | / | 27.3±0.8 | 7.8±0.9 | 0±0.11 | 8.1±0.2 | 78.2±2.3 | | -1.5±2.4 | |
| Placebo | 25 | 58.6±6.3 | / | 27.0±0.7 | 6.4±0.9 | 0.7±0.04 | 8.3±0.3 | 79.2±1.8 | | -1.3±1.8 | |
| Hanefeld, 2002[5](#_ENREF_5) | | 16 weeks | Acarbose 100mg tid | 11 | 60.4±1.3 | 91 | 27.5±0.7 | 7.7±1.3 | 0.4±0.6 | 8.2±0.3 | / | | / | |
| Glibenclamide 1mg tid | 8 | 60.6±2.5 | 62.5 | 27.1±1.1 | 7.1±1.2 | -0.8±0.6 | 8.4±0.4 | / | | / | |
| Placebo | 8 | 59±1.6 | 75 | 27.2±1.1 | 6.8±1.6 | 0.9±0.6 | 8.7±0.6 | / | | / | |
| Hanefeld, 2009[49](#_ENREF_49) | | 20 weeks | Acarbose 100mg tid | 42 | 62.33±8.7 | / | 31.02±5.12 | / | -0.07±0.55 | 6.11±0.48 | / | | / | |
| Placebo | 45 | 59.92±10.0 | / | 30.78±3.70 | / | -0.03±0.75 | 6.09±0.66 | / | | / | |
| Hasche, 1999[50](#_ENREF_50) | | 24 months | Acarbose 100mg tid | 52 | / | / | 26.9±3.1 | / | -1.71±1.6 | 8.9±0.8 | 74.9±8.7 | | -1.4±2.8 | |
| Placebo | 48 | / | / | 26.2±2.4 | / | -0.82±1.1 | 8.7±0.9 | 74.5±8.6 | | -1.3±3 | |
| Hoffmann, 1997[34](#_ENREF_34) | | 24 weeks | Acarbose 100mg tid | 31 | 58.9±9.4 | 19 | 26.4±2.7 | 3.0±2.3 | -1.1±0.9 | 9.6±0.9 | 73.9±10.3 | | -0.8±10.3 | |
| Metformin 850mg bid | 31 | 55.9±7.8 | 45 | 27.4±2.2 | 2.1±1.5 | -1.0±0.9 | 9.7±0.9 | 79±8.8 | | +0.2±8.8 | |
| Placebo | 32 | 60.2±8.6 | 38 | 26.3±2.2 | 3.6±2.8 | 0.4±0.9 | 9.4±0.9 | 74.9±9.7 | | -0.5±9.7 | |
| Hoffmann, 1994[6](#_ENREF_6) | | 24 weeks | Acarbose 100mg tid | 28 | 58.8±6.9 | 46 | 26.5±1.6 | 12.7±10.8 | -0.99±0.4 | 8.29±0.42 | / | | / | |
| Placebo | 30 | 56.9±6.7 | 40 | 26.8±1.5 | 12.1±10.8 | 0.11±0.3 | 8.29±0.37 | / | | / | |
| Hotta, 1993[51](#_ENREF_51) | | 24 weeks | Acarbose 100mg tid | 20 | 49.8 | 26.3 | / | 4.6 | -1.4±1 | 11.1 | / | | / | |
| Placebo | 20 | 47.9 | 22.2 | / | 4.4 | -0.4±1.0 | 10.3 | / | | / | |
| Josse, 2003[52](#_ENREF_52) | | 12 months | Acarbose 100mg tid | 93 | 69.7±0.5 | / | 28.3±0.4 | 5.8±0.7 | -0.3±0.1 | 7.4±0.1 | 79.4±1.3 | | / | |
| Placebo | 99 | 70.3±0.5 | / | 28.6±0.4 | 4.8±0.5 | 0.3±0.1 | 7.3±0.1 | 81.3±1.6 | | / | |
| Meneilly, 2000[53](#_ENREF_53) | | 12 months | Acarbose 100mg tid | 22 | 68±1 | / | 29.0±1.0 | / | -0.4±0.1 | 7.3±0.1 | / | | / | |
| Placebo | 23 | 70±1 | / | 28.0±1.0 | / | 0.4±0.2 | 7±0.2 | / | | / | |
| Rosenbaum, 2002[54](#_ENREF_54) | | 22 weeks | Acarbose 300mg qd | 20 | 59.8±8.2 | 30 | 30.3±2.9 | 6.8 | -0.8±1.98 | 6.4±1.7 | 75.1±11.6 | | / | |
| Placebo | 20 | 62±9.7 | 40 | 31.7±3.9 | 6.8 | 0±2.2 | 6.3±2.1 | 80.2±9.8 | | / | |
| Segal, 1997[9](#_ENREF_9) | | 24 weeks | miglitol | 40 | 61 | 55 | 28.6 | / | -0.60±1 | 7.95 | / | | -1.4±1 | |
| glibenclamide | 37 | 56 | 62.2 | 29.2 | / | -0.86±1 | 7.96 | / | | +1.4±1 | |
| PBO | 42 | 59 | 57.1 | 29.1 | / | 0.15±1 | 8.25 | / | | 0 | |
| Scott, 1999[55](#_ENREF_55) | | 16 weeks | Acarbose 100mg tid | 53 | 56±9 | 62 | 31.0±3.0 | 1.75±1.25 | -0.14±0.91 | 7.0±0.87 | 91±13 | | / | |
| Placebo | 52 | 57±8 | 65 | 29.0±3.0 | 2.17±1.42 | 0.25±1.15 | 6.89±0.85 | 84±12 | | / | |
| Wagner, 2006[56](#_ENREF_56) | | 12 weeks | Acarbose 100mg tid | 14 | 57(52-58) | 57.1 | 28.7  (26.3-29, 6) | 3.5(1-6) | -0.4±0.7 | 5.9±0.75 | 53.1 | | +0.2±1 | |
| Placebo | 17 | 54(50-58) | 82.3 | 28.7  (25.6-30.30) | 4(2-5) | -0.5±0.55 | 6.6±0.5 | 60.5 | | 0±1 | |
| **AGI versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Bachmann, 2003[57](#_ENREF_57) | | 78 weeks | Acarbose100mg tid +SU | 164 | 63.8±7.1 | 47.6 | 29.0±3.1 | 8±13.3 | -0.54±0.32 | 9.42±0.66 | 80.7±11.4 | | / | |
| Placebo+SU | 166 | 63.3±7.2 | 43.3 | 29.0±2.9 | 8±12.5 | 0±0.73 | 9.38±0.73 | 81.6±11.8 | | / | |
| Chiasson, 1994[46](#_ENREF_46) | | 1 year | Acarbose 200mg qd +MET | 41 | / | / | 29.4±0.6 | / | -0.6±0.2 | 7.8±0.2 | / | | / | |
| Placebo+MET | 42 | / | / | 29.4±0.6 | / | 0.3±0.2 | / | | / | |
| Acarbose 200mg qd +SU | 52 | / | / | 27.8±0.4 | / | -0.6±0.2 | 8±0.2 | / | | / | |
| Placebo+SU | 51 | / | / | 27.8±0.4 | / | 0.3±0.2 | / | | / | |
| Acarbose 200mg qd +insulin | 41 | / | / | 30.2±0.5 | / | -0.5±0.2 | 7.7±0.2 | / | | / | |
| Placebo+insulin | 50 | / | / | 30.2±0.5 | / | -0.1±0.2 | / | | / | |
| Chiasson, 2001[25](#_ENREF_25) | | 36 weeks | Placebo+MET | 83 | 57.9±8.6 | 73.5 | 30.7±5.1 | 7.5±7.4 | -0.85±0.12 | 8.2±0.9 | 88.6±14.1 | | -0.69±0.27 | |
| Miglitol+MET | 76 | 58.9±7.9 | 77.6 | 29.5±3.8 | 6.1±5.5 | -1.39±0.11 | 8.3±0.8 | 91±15.5 | | -0.42±0.29 | |
| Halimi, 2000[58](#_ENREF_58) | | 6 months | Acarbose 100mg tid +MET | 59 | 56±9.2 | 47.4 | 30.1±3.3 | 9.5±7.4 | -0.7±1.2 | 8.6±1.1 | / | | / | |
| Placebo+MET | 70 | 55±10 | 62.8 | 29.7±3.3 | 9±7.5 | 0.2±1.3 | 8.5±1.1 | / | | / | |
| Hsieh, 2011[59](#_ENREF_59) | | 24 weeks | Miglitol 100mg tid+SU | 52 | 58.4±10.5 | 79.3 | / | / | -0.85±0.12 | 8.14±0.72 | 67.2±10.3 | | / | |
| Placebo+SU | 53 | 59±10.7 | 51.4 | / | / | -0.19±0.11 | 8.11±0.77 | 69.2±10.6 | | / | |
| Hwu, 2003[60](#_ENREF_60) | | 18 weeks | Acarbose 100mg tid+INS | 54 | 58.1±8.4 | / | / | 13.4±9.1 | -0.5±1.3 | 9.5±0.8 | 62±9.6 | | +0.3±1.5 | |
| Placebo+INS | 53 | 54.7±8.6 | / | / | 10.9±6.1 | 0.2±1.2 | 9.5±1 | 61.4±12.1 | | -0.1±2.3 | |
| Kelley, 1998[61](#_ENREF_61) | | 24 weeks | Acarbose 100mg tid+insulin | 72 | 61.8 | 63 | 31 | 12.5 | -0.58±0.1 | 8.77 | 91.4 | | -0.58±1 | |
| Placebo+insulin | 73 | 60.8 | 48 | 31.1 | 12.3 | 0.11±0.1 | 8.69 | 88.8 | | 0.11±1 | |
| Johnston, 1998 [62](#_ENREF_62) | | 1 year | Miglitol 100mg tid±SU | 204 | 55±1 | 50 | 31.9±0.1 | 5.1±0.5 | -0.21±0.15 | 8.69±0.14 | / | | / | |
| Placebo±SU | 105 | 56.9±1.3 | 51 | 32.0±0.9 | 4.5±0.7 | 0.53±0.21 | 8.62±0.18 | / | | / | |
| Johnston, 1998-2[63](#_ENREF_63) | | 1 year | Miglitol 200mg tid±SU | 220 | 52.9 | / | 31.8 | 5.7 | -0.26±1 | 8.7 | 85.8 | | / | |
| Placebo±SU | 120 | 53.9 | / | 30.6 | 4.8 | 0.57±1 | 8.53 | 82.9 | | / | |
| Lin BJ, 2003[64](#_ENREF_64) | | 24 weeks | Acarbose 100mg tid+SU | 32 | 57.7±7.3 | 53.1 | / | 7 | -0.92±1.69 | 9.01±1.2 | 63.9±7.2 | | / | |
| Placebo+SU | 32 | 55.4±8.5 | 37.5 | / | 5 | 0.13±1.43 | 8.99±0.95 | 61.6±7.9 | | / | |
| Lam KSL, 1998[65](#_ENREF_65) | | 24 weeks | Acarbose 100mg tid+SU+met | 45 | 57.8±1.3 | 44.4 | 24.8±0.5 | 10.2±0.7 | -0.5±0.2 | 9.5±0.1 | / | | -0.54±0.32 | |
| Placebo+SU+met | 44 | 56.9±1.3 | 43.2 | 24.1±0.4 | 10.1±0.8 | 0.1±0.2 | 9.4±0.1 | / | | +0.42±0.29 | |
| Mitrakou,1998[66](#_ENREF_66) | | 24 weeks | Miglitol 100mg tid+insulin | 60 | 57.4±5.6 | 48.3 | 24.4±3.1 | 8.5±4.5 | -1.6±0.7 | 9.9±0.5 | 67.3±6.2 | | +0.6±6 | |
| Placebo+ insulin | 60 | 57.4±5.8 | 61.7 | 24.5±3.4 | 7.9±3.2 | -0.3±0.6 | 9.9±0.4 | 68.9±7.3 | | +0.2±7.5 | |
| Nemoto, 2011[67](#_ENREF_67) | | 12 weeks | Miglitol 50mg tid+insulin | 107 | / | / | / | / | -0.37±0.68 | 7.85±1.02 | / | | / | |
| Placebo+insulin | 100 | / | / | / | / | 0.04±0.56 | / | | / | |
| Phillips, 2003[68](#_ENREF_68) | | 24 weeks | Acarbose 100mg bid +MET | 40 | 58.37±10.7 | 65 | 30.75±2.96 | 5.32±4.55 | -0.16±0.18 | 8.05±0.89 | 89.77±12.73 | | -1.32±2.37 | |
| Placebo+MET | 43 | 62.39±8.02 | 76.7 | 30.09±2.85 | 6.06±5.32 | 0.86±0.16 | 7.82±0.83 | 87.88±11.7 | | -0.43±2.9 | |
| Schnell, 2007[69](#_ENREF_69) | | 20 weeks | Acarbose 100mg tid+insulin | 82 | 61.5±8.9 | / | 30.4±4.2 | 11.5±7 | -2.31±1.61 | 9.8±1.5 | 85.44±13.64 | | -0.25±20.73 | |
| Placebo+insulin | 81 | 62.3±7.4 | / | 29.9±4.5 | 9.6±5.1 | -1.81±1.11 | 9.4±1 | 84.41±13.18 | | 10.36±13.68 | |
| Standl, 1999[70](#_ENREF_70) | | 24 weeks | Acarbose 200mg tid+insulin | 24 | 59.3±8.5 | / | 25.2±2.2 | 11.5±6.8 | -2.4±1.0 | 10.9±1 | 70.5±11.7 | | +1.7±11.7 | |
| Placebo+insulin | 24 | 62.9±9.4 | / | 24.1±2.0 | 12.2±5.7 | -2.4±1.0 | 11.0±1.2 | 66.7±10.8 | | +1.5±10.8 | |
| Standl, 2001[71](#_ENREF_71) | | 24 weeks | Miglitol 100mg tid+SU+MET | 65 | 62±8 | 50.8 | 27.7±3.7 | 8 | -0.55±1.02 | 8.83±0.85 | 79±13 | | / | |
| Placebo+ SU+MET | 68 | 61±8 | 54.4 | 27.9±3.5 | 9 | -0.2±1.07 | 8.84±0.66 | 82±15 | | / | |
| Willms, 1999[72](#_ENREF_72) | | 12 weeks | Acarbose 100mg tid+SU | 31 | 60.3±8.8 | 48.4 | / | 10.4±6.8 | -2.3±0.32 | 10.6±1.3 | 86.±15.4 | | -3.5±15.4 | |
| Metformin 850mg bid+SU | 29 | 53.4±8.2 | 48.1 | / | 9.3±6.9 | -2.5±0.16 | 10.6±1.4 | 88.6±17.7 | | -1.4±17.7 | |
| Placebo+ SU | 29 | 59.2±9.4 | 58.6 | / | 10.0±6.4 | -1.3±0.34 | 10.6±1.6 | 90.2±15.4 | | -1±15.4 | |
| Van Gaal, 2001[73](#_ENREF_73) | | 32 weeks | Miglitol 100mg tid+MET | 77 | 57.9±10 | 41.5 | 30.0±4.0 | 6 | -0.21±1.13 | 8.5±1 | / | | -2.5±3.8 | |
| Placebo+ MET | 75 | 57.9±8.5 | 49.3 | 29.7±3.9 | 6 | 0.22±1.17 | 8.4±1 | / | | -0.7±2.5 | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **TZD versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Aronoff, 2000[74](#_ENREF_74) | | 26 weeks | pioglitazone 7.5mg | 80 | / | / | / | / | 0.2±0.17 | 10.0±0.22 | 93.5±1.59 | | -0.6±0.29 | |
| pioglitazone 15mg | 79 | / | / | / | / | -0.3±0.17 | 10.2±0.22 | 91.2±1.80 | | 1.3±0.33 | |
| pioglitazone 30mg | 85 | 53.7 | / | / | / | -0.3±0.17 | 10.2±0.21 | 90.3±1.58 | | 1.3±0.38 | |
| pioglitazone 45mg | 76 | / | / | / | / | -0.9±0.18 | 10.3±0.22 | 90.8±1.56 | | 2.8±0.39 | |
| placebo | 79 | 53.7 | / | / | / | 0.7±0.17 | 10.4±0.22 | 90.4±1.47 | | -1.3±0.36 | |
| Carey, 2002[75](#_ENREF_75) | | 16 weeks | rosiglitazone 8mg/day | 16 | 54.2±11.1 | 87.5 | 29.8±4.0 | 3.3±4.5 | -0.7±0.7 | 7.8±1.3 | 93.9±14.1 | | 2.1±2.0 | |
| placebo | 17 | 57.9±10.7 | 76.5 | 31.3±3.6 | 3.1±3.3 | 0.4±1.0 | 7.1±1.4 | 89.5±12.5 | | 0.1±1.8 | |
| Chou, 2012[76](#_ENREF_76) | | 26 weeks | rivoglitazone 1.0mg/day | 274 | 55.0±10.51 | 48.2 | 29.7±5.63 | 5.0±5.26 | -0.4±0.05 | 7.7±0.53 | 80.5±19.65 | | +2.3±19.65 | |
| rivoglitazone 1.5mg/day | 750 | 55.1±10.59 | 50.9 | 29.6±5.27 | 4.3±4.40 | -0.7±0.03 | 7.7±0.57 | 80.6±17.67 | | +3.4±17.67 | |
| pioglitazone 45mg/day | 751 | 55.0±10.84 | 53 | 30.0±5.80 | 4.4±4.99 | -0.6±0.03 | 7.7±0.58 | 81.6±19.59 | | +2.7±19.59 | |
| placebo | 137 | 55.4±12.32 | 48.9 | 30.1±5.43 | 4.9±6.13 | 0.2±0.06 | 7.7±0.54 | 82±19.73 | | -0.8±19.73 | |
| Ebeling, 1999[77](#_ENREF_77) | | 16 weeks | Troglitazone 400mg qd | 15 | 62.6±2.2 | 33.3 | 32.3±1.3 | 15.9±2.1 | -1.2±0.3 | 8.7±0.3 | / | | / | |
| placebo | 12 | 63.5±2.8 | 50 | 33.1±1.0 | 14.3±1.9 | -0.1±0.3 | 8.8±0.3 | / | | / | |
| Ebeling, 2001[2](#_ENREF_2) | | 6 months | Pioglitazone 30mg qd | 9 | 55.2 | / | 30.5±1.3 | 5.9 | -1.1±0.5 | 9.1±0.3 | / | | / | |
| glibenclamide | 10 | 55.2 | / | 30.2±1.7 | 5.9 | -1.2±0.3 | 8.9±0.3 | / | | / | |
| PBO | 10 | 55.2 | / | 31.9±1.5 | 5.9 | -0.2±0.3 | 8.6±0.2 | / | | / | |
| Fonseca, 1998[78](#_ENREF_78) | | 26 weeks | Troglitazone 100mg | 17 | 54±11 | 59.2 | 32.4±6.6 | 5.3±5.6 | 9.2±2.0 | 0.48±0.41 | / | | / | |
| Troglitazone 200mg | 18 | 8.3±1.5 | -0.24±0.40 | / | | / | |
| Troglitazone 400mg | 19 | 8.5±2.1 | 0.34±0.36 | / | | / | |
| Troglitazone 600mg | 15 | 8.6±2.2 | -0.95±0.42 | / | | / | |
| Placeboo | 18 | 8.7±1.9 | 0.40±0.40 | / | | / | |
| Fonseca, 1998[79](#_ENREF_79) | | 26 weeks | Troglitazone 600mg qd | 18 | 60.4±5.9 | 44.4 | 37.3±9.2 | / | 0.3±2 | 9.5±2 | / | | / | |
| placebo | 8 | 52.6±7.5 | 37.5 | 39.6±13.4 | / | 0.8±1.3 | 10.1±1.43 | / | | / | |
| Gastaldelli, 2006[80](#_ENREF_80) | | 12 weeks | rosiglitazone 8mg/day | 13 | 53±2 | 53.8 | 29.3±1.2 | 4±2 | -1.1±0.5 | 8.6±0.5 | / | | / | |
| PBO | 13 | 56±2 | 61.5 | 30.2±1.0 | 3±1 | 0.4±0.4 | 8.2±0.4 | / | | / | |
| Gastaldelli, 2007-1[81](#_ENREF_81) | | 4 months | rosiglitazone 8mg/day | 12 | 55±3 | 50 | 29.2±1.3 | 4±2 | -1.4±0.5 | 8.7±0.5 | / | | / | |
| PBO | 12 | 56±2 | 66.7 | 29.8±1.2 | 2±1 | 0.6±0.5 | 8.1±0.4 | / | | / | |
| Haffner, 2002[82](#_ENREF_82) | | 26 weeks | rosiglitazone 4mg/day | 126 | 60.7±9.3 | 53.2 | 30.3±4.1 | 4.7±6.1 | -0.6±1.2 | 8.8±1.4 | / | | / | |
| rosiglitazone 8mg/day | 136 | 60.4±9.3 | 47.8 | 29.5±3.8 | 4.9±5.2 | -0.9±1.2 | 8.6±1.5 | / | | / | |
| PBO | 95 | 59.8±10.5 | 61.1 | 30.1±3.9 | 4.5±4.8 | 0.6±1.1 | 8.7±1.5 | / | | / | |
| Hällsten, 2002[32](#_ENREF_32) | | 26 weeks | Rosiglitzone 4mg bid | 14 | 58.6±2.0 | 71.4 | 29.3±1.0 | / | -0.3±0.2 | 6.8±0.2 | / | | / | |
| metformin | 13 | 57.8±2.2 | 61.5 | 29.9±1.1 | / | -0.7±0.2 | 6.9±0.2 | / | | / | |
| PBO | 14 | 57.7±1.9 | 71.4 | 30.3±1.2 | / | -0.2±0.1 | 6.3±0.1 | / | | / | |
| Iwamoto, 1996[83](#_ENREF_83) | | 12 weeks | troglitazone 400mg/day | 136 | 54.6±10.1 | 50.7 | 24.1±3.5 | 6.3±4.4 | -0.5±1.7 | 8.61±1.51 | 61±11 | | 0.6±1.6 | |
| PBO | 126 | 57.4±9.3 | 53.2 | 24.7±3.4 | 7.5±5.4 | 0.1±1.6 | 8.51±1.46 | 61.8±10.4 | | -0.4±1.2 | |
| Juhl, 2003[84](#_ENREF_84) | | 13 weeks | rosiglitazone 4mg bid | 10 | 54±9 | 90 | 30.0±2.7 | / | -0.3±1.2 | 7.0±1.4 | 92±7 | | +2±8 | |
| PBO | 10 | 54±9 | 60 | 31.7±1.9 | / | 0.1±1.1 | 6.8±1.0 | 95±10 | | -0.3±10 | |
| Khan, 2006[85](#_ENREF_85) | | 26 weeks | pioglitazone 15mg | 22 | 56.4±9.95 | 63.6 | 31.8±3.67 | / | -0.70±0.279 | 8.46±0.309 | 93.7±18.09 | | / | |
| pioglitazone 30mg | 22 | 52.7±8.95 | 68.2 | 32.3±4.48 | / | -0.91±0.282 | 8.45±0.312 | 95.3±14.96 | | / | |
| pioglitazone 45mg | 23 | 56.7±7.17 | 60.9 | 30.7±3.05 | / | -1.63±0.297 | 9.54±0.326 | 90.3±13.06 | | / | |
| PBO | 21 | 54.8±8.65 | 28.6 | 32.0±4.23 | / | 0.66±0.289 | 8.62±0.323 | 89.3±11.25 | | / | |
| Kong, 2011[86](#_ENREF_86) | | 12 weeks | rivoglitazone 0.5mg | 35 | 53.9±7.6 | 54.3 | 26.05±4.51 | 4.39±3.66 | -0.11±0.85 | 7.46±0.72 | 67.5±13.83 | | / | |
| rivoglitazone 1.0mg | 35 | 53.2±7.8 | 57.1 | 25.6±3.72 | 4.87±3.14 | -0.22±0.74 | 7.45±0.72 | 65.34±13.11 | | / | |
| rivoglitazone 1.5mg | 34 | 52.4±9.3 | 55.9 | 25.97±4.17 | 4.36±3.74 | -0.17±0.87 | 7.4±0.70 | 68.91±13.13 | | / | |
| pioglitazone 30mg | 37 | 53.6±7.6 | 56.8 | 24.86±3.26 | 5.59±4.60 | -0.06±0.86 | 7.49±0.82 | 64.09±10.79 | | / | |
| PBO | 32 | 54.0±8.5 | 59.4 | 25.53±4.03 | 5.85±3.89 | 0.61±0.99 | 7.35±0.62 | 67.71±13.7 | | / | |
| Kumar, 1996[87](#_ENREF_87) | | 12 weeks | troglitazone 200mg qd | 48 | 59 | 64.6 | 28.5±4.1 | 5 | -0.3±1 | 7.6 | / | | / | |
| troglitazone 400mg qd | 41 | 58 | 58.5 | 28.4±3.9 | 7 | 0.3±1 | 7.1 | / | | / | |
| troglitazone 600mg qd | 47 | 60 | 57.4 | 28.6±5.3 | 6 | 0±1 | 7.2 | / | | / | |
| troglitazone 800mg qd | 50 | 56 | 64 | 28.3±4.4 | 5 | 0±1 | 7 | / | | / | |
| troglitazone 200mg bid | 45 | 57 | 68.9 | 29.3±4.3 | 6 | -0.2±1 | 7.3 | / | | / | |
| troglitazone 400mg bid | 49 | 56 | 57.1 | 27.7±4.0 | 6 | 0.2±1 | 6.9 | / | | / | |
| PBO | 49 | 57 | 73.5 | 28.9±4.6 | 7 | 0.8±1 | 7.2 | / | | / | |
| Lautamäki, 2005[88](#_ENREF_88) | | 16 weeks | Rosiglitazone 8mg qd | 27 | 64.1±7.8 | 70.4 | 29.6±4.7 | 6.7±6.4 | -0.4±0.9 | 7.3±0.9 | 85.3±17.4 | | / | |
| PBO | 27 | 63.2±7.4 | 70.4 | 29.6±3.4 | 6.8±5.9 | 0.2±1.0 | 7.1±0.9 | 89.1±14.3 | | / | |
| Miyazaki, 2001[89](#_ENREF_89) | | 12 weeks | rosiglitazone 8mg/day | 15 | 54 | 46.7 | 30.0±1.1 | 6 | -1.3±0.3 | 8.7±0.4 | 86±4 | | 3.7±0.8 | |
| PBO | 14 | 56 | 62.3 | 30.1±1.0 | 4 | 0.5±0.3 | 8.3±0.4 | 87±5 | | 0±0.4 | |
| Miyazaki, 2001[90](#_ENREF_90) | | 16 weeks | pioglitazone 45mg/day | 12 | 54 | 91.7 | 28.7±1.1 | 5.8 | -1.7±0.3 | 8.9±0.3 | 84.8±3.6 | | 3.6±1.4 | |
| PBO | 11 | 55 | 54.5 | 29.5±1.3 | 4.7 | 0±0.2 | 7.9±0.3 | 81.4±5 | | 0.3±0.4 | |
| Miyazaki, 2002[91](#_ENREF_91) | | 26 weeks | pioglitazone 7.5mg | 13 | 51±3 | 76.9 | 31.3±1.2 | / | 0.3±0.4 | 8.9±0.4 | 93±5 | | 0.2±0.5 | |
| pioglitazone 15mg | 12 | 57±4 | 66.7 | 30.8±1.3 | / | -0.1±0.4 | 8.0±0.3 | 93±5 | | 2±0.9 | |
| pioglitazone 30mg | 11 | 51±2 | 72.7 | 32.2±1.6 | / | -0.8±0.3 | 8.5±0.5 | 97±4 | | 3±1.1 | |
| pioglitazone 45mg | 11 | 55±2 | 45.5 | 30.4±1.0 | / | 1.8±0.4 | 9.1±0.3 | 86±3 | | 4.5±0.7 | |
| PBO | 11 | 58±3 | 27.3 | 32.8±1.6 | / | 1.2±0.5 | 8.6±0.5 | 90±4 | | -0.4±1,4 | |
| Nakamura, 2001[92](#_ENREF_92) | | 6 months | pioglitazone 30mg/day | 14 | / | / | / | / | -2.2±1.3 | 8.4±1.3 | / | | / | |
| PBO | 14 | / | / | / | / | 0.1±1.3 | 8.0±1.0 | / | | / | |
| Natali, 2004[37](#_ENREF_37) | | 16 weeks | metformin | 28 | 58±10 | 78.6 | 28.0±3.5 | 6.3±5.3 | -0.33±1.1 | 7.8±1.1 | 77.3±12.5 | | -0.6±0.4 | |
| Rosiglitazone 8mg qd | 24 | 59±7 | 91.7 | 27.6±2.8 | 6.5±4.5 | 0.09±1.2 | 7.2±1.2 | 80.4±10.1 | | 0.5±0.5 | |
| PBO | 22 | 58±9 | 81.8 | 30.2±3.1 | 3.4±3.4 | 1.3±0.8 | 7.6±0.8 | 86.9±10.5 | | -0.3±0.8 | |
| Oz Gul, 2008[93](#_ENREF_93) | | 12 weeks | pioglitazone 30mg/day | 14 | / | / | 29.3±2.9 | / | -1.22±1.6 | 7.82±1.7 | / | | / | |
| rosiglitazone 4mg/day | 11 | 55.2 | / | 28.3±4.09 | / | -0.8±1 | 7.0±1.07 | / | | / | |
| PBO | 10 | 55.2 | / | 29.2±2.3 | / | 0.06±1.0 | 6.39±1.1 | / | | / | |
| Oz Gul, 2010[94](#_ENREF_94) | | 12 weeks | pioglitazone 30mg/day | 19 | / | / | 29.3±3.0 | / | -1.1±1.4 | 7.6±1.5 | / | | / | |
| rosiglitazone 4mg/day | 20 | 56.4 | / | 29.6±4.8 | / | -1.1±1.3 | 7.3±1.3 | / | | / | |
| PBO | 21 | 56.4 | / | 29.6±4.1 | / | -0.1±0.9 | 7.3±0.9 | / | | / | |
| Patel, 1999[95](#_ENREF_95) | | 12 weeks | rosiglitazone 0.05mg bid | 74 | 56.7±12.33 | 66.2 | 29.4±3.76 | 4.9 | 0.6±0.14 | 9.1 | / | | / | |
| rosiglitazone 0.25mg bid | 72 | 55.8±11.75 | 70.8 | 28.6±4.11 | 6.7 | 0.6±0.14 | 8.9 | / | | / | |
| rosiglitazone 1.0mg bid | 79 | 59.8±9.51 | 64.6 | 29.5±4.06 | 4.4 | 0.1±0.13 | 9 | / | | / | |
| rosiglitazone 2.0mg bid | 80 | 59.7±10.0 | 68.8 | 28.4±4.09 | 5.8 | -0.1±0.13 | 9 | / | | / | |
| PBO | 75 | 56.8±11.50 | 69.3 | 28.9±3.98 | 4.2 | 0.3±0.13 | 9.1 | / | | / | |
| Phillips, 2001[96](#_ENREF_96) | | 16 weeks | rosiglitazone 4mg Qd | 181 | 57.5±9.9 | 58.6 | 29.9±4.1 | 5.4±6.1 | 0±1.6 | 8.9±1.6 | / | | / | |
| rosiglitazone 2mg bid | 186 | 56.8±9.4 | 59.1 | 30.0±4.2 | 5.5±4.9 | -0.1±1.5 | 8.9±1.5 | / | | / | |
| rosiglitazone 8mg Qd | 181 | 58.9±9.9 | 65.7 | 30.0±4.3 | 6.1±6.7 | -0.3±1.5 | 8.9±1.5 | / | | / | |
| rosiglitazone 4mg bid | 187 | 56.5±9.7 | 65.2 | 29.9±4.3 | 5.9±6.1 | -0.7±1.5 | 9.0±1.5 | / | | / | |
| PBO | 173 | 57.7±9.2 | 68.8 | 29.1±4.2 | 6.6±6.9 | 0.8±1.5 | 8.9±1.5 | / | | / | |
| Raskin, 2000[97](#_ENREF_97) | | 8 weeks | rosiglitazone 2mg bid | 73 | 58.47±9.80 | 61.6 | 30.15±4.68 | 5.6±5.93 | 0.4±1.8 | 8.7±1.44 | / | | / | |
| rosiglitazone 4mg bid | 66 | 57.02±10.0 | 60.6 | 30.49±3.76 | 4.0±4.70 | / | 8.9±1.45 | / | | / | |
| rosiglitazone 6mg bid | 76 | 58.61±10.05 | 60.5 | 30.02±4.38 | 6.0±5.81 | / | 8.7±1.49 | / | | / | |
| PBO | 69 | 60.06±9.39 | 59.4 | 30.44±4.15 | 5.6±5.19 | 1.0±2.0 | 8.7±1.63 | / | | / | |
| Rosenblatt, 2001[98](#_ENREF_98) | | 16 weeks | pioglitazone 30mg Qd | 101 | 53.8±10.0 | 50.5 | 31.5±4.7 | / | -0.6±0.17 | 10.65±1.77 | 89.8±18.0 | | +1.35±18.0 | |
| PBO | 96 | 55.2±10.0 | 56.2 | 30.7±5.0 | / | 0.76±0.17 | 10.42±1.70 | 87.2±18.4 | | -1.87±18.4 | |
| Rosenstock, 2002[99](#_ENREF_99) | | 16 weeks | troglitazone 600mg/day | 150 | 58 | 59 | 21-38 | 0.1-33.4 | -0.8±1 | 8.4±1.1 | / | | / | |
| nateglinide 120mg/day | 151 | 57 | 63 | 19-37 | 0-20.4 | -0.6±1 | 8.1±1.0 | / | | / | |
| nateglinide 120mg/day  +troglitazone 600mg/day | 150 | 59 | 61 | 21-45 | 0.3-26.2 | -1.7±1.3 | 8.3±1.3 | / | | / | |
| PBO | 148 | 58 | 59 | 20-38 | 0.2-37.9 | 0.5±1.0 | 8.2±1.2 | / | | / | |
| Scherbaum, 2002[100](#_ENREF_100) | | 26 weeks | pioglitazone 15mg Qd | 89 | 58 | 62.9 | 29.9 | 5.4 | -0.92±1.50 | 9.33 | 87.2 | | / | |
| pioglitazone 30mg Qd | 78 | 59.6 | 41 | 29.3 | 4.6 | -1.05±1.25 | 9.06 | 82.0 | | / | |
| PBO | 84 | 59.1 | 56 | 29.2 | 5.6 | -0.34±0.98 | 8.75 | 84.8 | | / | |
| Sourij, 2006[101](#_ENREF_101) | | 12 weeks | pioglitazone 30mg/day | 21 | / | / | / | / | 0±0.6 | 6.1±0.6 | / | | / | |
| PBO | 21 | / | / | / | / | -0.2±0.5 | 6.1±0.5 | / | | / | |
| Truitt, 2010[102](#_ENREF_102) | | 26 weeks | rivoglitazone 1mg Qd | 87 | 55.4±10.9 | 52.9 | 32.9±6.0 | 6.2±6.4 | 0.02±0.13 | 8.00±0.81 | 93.3±20.7 | | 1.2±20.7 | |
| rivoglitazone 2mg Qd | 85 | 55.0±10.8 | 56.5 | 33.1±6.4 | 5.2±4.5 | -0.43±0.13 | 8.05±0.87 | 96.3±18.7 | | 3.0±18.7 | |
| rivoglitazone 3mg Qd | 86 | 56.4±10.8 | 52.3 | 33.0±6.5 | 6.7±7.3 | -0.54±0.14 | 8.23±1.02 | 95.8±23.5 | | 4.1±23.5 | |
| pioglitazone 45mg Qd | 91 | 56.6±10.1 | 58.2 | 32.9±5.7 | 6.6±7.5 | -0.03±0.13 | 7.98±0.83 | 94.9±21.5 | | 2.1±21.5 | |
| PBO | 92 | 55.3±9.3 | 51.1 | 32.2±5.8 | 6.7±5.6 | 0.56±0.13 | 8.21±0.98 | 92.9±20.4 | | -1.4±20.4 | |
| Viljanen, 2005[39](#_ENREF_39) | | 26 weeks | Rosiglitazone 4mg bid | 14 | 58.6±7.7 | 64.3 | 29.3±4.0 | 6.8±0.9 | -0.3±0.9 | 6.8±0.9 | / | | / | |
| Metformin 1g bid | 12 | 57.8±8.7 | 58.3 | 29.6±4.0 | 6.9±0.9 | -0.3±0.9 | 6.9±0.9 | / | | / | |
| PBO | 11 | 58.7±8.3 | 81.8 | 29.8±4.1 | 6.2±0.7 | -0.1±0.7 | 6.2±0.7 | / | | / | |
| Wallace, 2004[103](#_ENREF_103) | | 12 weeks | Pioglitazone 45mg qd | 19 | 61.4±6.3 | 73.7 | 29.8±4.5 | 2.6 | -0.3±0.1 | 6.7±0.9 | 90.7±3.6 | | 0.7±0.6 | |
| PBO | 11 | 62.6±10.0 | 72.7 | 28.9±2.8 | 2.5 | 0.3±0.1 | 6.7±0.9 | 85.2±4.3 | | 1.1±0.5 | |
| **TZD versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Barnett, 2003[104](#_ENREF_104) | | 26 weeks | rosiglitazone 8mg/day  +sulphonylurea | 84 | 54.3 | 80 | 26.8 | 6.5 | -1.16±1.3 | 9.21±1.27 | / | | / | |
| placebo+sulphonylurea | 87 | 54.1 | 75 | 26.4 | 6.5 | 0.26±1.3 | 9.06±1.3 | / | | / | |
| Berhanu, 2007[105](#_ENREF_105) | | 20 weeks | Pioglitazone 45mg qd+insulin±metformin | 110 | 52.9±11.33 | 43.6 | 30.7±6.09 | 7.7±6.15 | -1.6±0.11 | 8.4±0.13 | / | | +4.39±1 | |
| placebo+insulin±metformin | 112 | 52.5±11.07 | 41.1 | 31.8±6.2 | 8.5±5.43 | -1.4±0.11 | 8.6±0.13 | / | | +2.42±1 | |
| Bertrand, 2010[106](#_ENREF_106) | | 12 months | Rosiglitazone 4mg bid | 98 | 64.2±7.3 | 92 | 30.2±4.2 | 7.8±6.4 | -0.5±1.2 | 6.9±1.3 | 85.9±14 | | 2.9±14 | |
| placebo | 95 | 65.9±6.9 | 92 | 29.5±4.6 | 8.4±6.9 | 0.1±0.9 | 6.9±0.8 | 83.9±15.1 | | 0.4±15 | |
| Brackenridge, 2009[107](#_ENREF_107) | | 3 months | rosiglitazone 8mg±metformin | 8 | 66.5±2.51 | 50 | 30.0±1.5 | 4.4±1.03 | -0.4±0.3 | 6.9±0.3 | 92±6.52 | | +0.6±6.52 | |
| pioglitazone 30mg±metformin | 8 | 61.0±3.93 | 87.5 | 30.8±1.26 | 4.0±0.8 | -0.7±0.2 | 7.5±0.21 | 96.4±3.62 | | +1.9±3.62 | |
| placebo±metformin | 8 | 60.8±3.45 | 87.5 | 32.0±1.56 | 2.9±0.4 | 0.2±0.2 | 6.6±0.14 | 103.9±5.61 | | +0.5±5.61 | |
| Buras, 2005[108](#_ENREF_108) | | 12 weeks | troglitazone 600mg | 33 | 58±9 | 60.6 | 30.9±5.3 | 8±8 | -0.6±0.75 | 7.6±1.4 | / | | 2.3±2.5 | |
| placebo | 39 | 57±9 | 66.7 | 32.6±5.0 | 8±9 | 0.1±0.45 | 7.9±1.4 | / | | 0.5±1.25 | |
| Buse, 1998[109](#_ENREF_109) | | 26 weeks | troglitazone 200mg | 75 | 58±9 | 59 | 34.4±6.2 | / | / | 9.5±1.7 | 98.9±18.1 | | -0.03±0.44 | |
| troglitazone 400mg | 76 | 58±10 | 50 | 34.8±6.7 | / | -0.4±1.4 | 9.0±1.4 | 98.9±20.2 | | +0.6±0.44 | |
| placebo | 71 | 57±11 | 49 | 34.5±7.2 | / | -0.1±1.4 | 9.0±1.4 | 98.9±22.4 | | -0.9±0.44 | |
| Buysschaert, 1999[110](#_ENREF_110) | | 16 weeks | troglitazone 100mg+SU | 84 | 59 | 63.1 | / | 8.47 | -0.6±1 | 8.3 | / | | / | |
| troglitazone 200mg+SU | 90 | 60 | 66.7 | / | 6.43 | -0.5±1 | 7.9 | / | | / | |
| placebo+SU | 85 | 60 | 51.8 | / | 7.77 | -0.3±1.0 | 8.5 | / | | / | |
| Charpentier, 2009[111](#_ENREF_111) | | 7 months | pioglitazone 30/45mg | 142 | 60.2±9.3 | 64.6 | 29.1±3.3 | 12.5±9.0 | -0.83±0.7 | 8.1±0.7 | 82 | | +1.8±1 | |
| placebo | 147 | 59.2±9.6 | 66.2 | 29.2±3.1 | 12.1±7.9 | +0.22±0.6 | 8.2±0.6 | 82.5 | | -0.2±1 | |
| Colca, 2013[112](#_ENREF_112) | | 12 weeks | 50mg MSDC-0160 | 48 | 56 | 50 | / | / | -0.1±1 | 8.18 | 91 | | / | |
| 100mg MSDC-0160 | 52 | 56 | 52 | / | / | -0.48±1 | 8.04 | 86 | | / | |
| 150mg MSDC-0160 | 47 | 55 | 68 | / | / | -0.5±1 | 8.01 | 94 | | / | |
| 45mg pioglitazone | 55 | 55 | 56 | / | / | -0.7±1 | 8.15 | 88 | | / | |
| placebo | 56 | 53 | 48 | / | / | 0.3±1.0 | 7.98 | 88 | | / | |
| Dailey, 2004[113](#_ENREF_113) | | 24 weeks | Rosiglitazone 8mg qd＋glyburide/metformin | 181 | 57±9 | 58 | 32±5 | 9±7 | -0.9±0.9 | 8.1±0.9 | 93±18 | | 3±18 | |
| placebo＋glyburide/metformin | 184 | 57±10 | 61 | 32±5 | 9±6 | 0.1±0.8 | 8.1±0.8 | 93±18 | | 0.03±18 | |
| Davidson, 2007[114](#_ENREF_114) | | 24 weeks | Rosiglitazone 8mg qd+glyburide | 117 | 52±11.9 | 45.3 | 31.3±5.7 | 6.0±5.2 | -1.2±0.2 | 9.2±1.3 | 86.3±18.8 | | 4.3±3.5 | |
| placebo+ glyburide | 116 | 53±10.4 | 48.3 | 31.9±5.6 | 6.2±5.3 | 0.14±0.2 | 9.4±1.4 | 88.3±19.4 | | 0.1±2.4 | |
| Derosa, 2008[115](#_ENREF_115) | | 6 months | Rosiglitazone 8mg qd+metformin | 56 | 55±4 | 46.4 | 28.6±1.9 | 3±1 | -1.4±0.6 | 7.8±0.7 | / | | / | |
| placebo+metformin | 61 | 54±3 | 47.5 | 28.4±1.7 | 4±1 | -0.6±0.8 | 8.0±0.9 | / | | / | |
| Fonseca, 2000[116](#_ENREF_116) | | 26 weeks | metformin 2.5g/d+placebo | 113 | 58.8±9.2 | 74.3 | 30.3±4.4 | 7.3±5.7 | 0.45±1.2 | 8.6±1.3 | / | | / | |
| metformin 2.5g/d+RSG 4mg/d | 116 | 57.5±10.5 | 62.1 | 30.2±4.2 | 7.5±6.3 | -0.56±1.3 | 8.9±1.3 | / | | / | |
| metformin 2.5g/d+RSG 8mg/d | 110 | 58.3±8.8 | 68.2 | 29.8±3.9 | 8.3±6.3 | -0.78±1.5 | 8.9±1.5 | / | | / | |
| Galle, 2012[117](#_ENREF_117) | | 6 months | pioglitazone 30mg+insulin | 20 | 68.9±6.8 | 70 | 31.5±4.0 | 13.8±9.8 | -0.6±0.87 | 7.4±0.9 | / | | / | |
| placebo+insulin | 19 | 69.6±9.4 | 68.4 | 30.3±4.6 | 12.4±8.2 | 0.21±1.1 | 7.7±0.9 | / | | / | |
| Gastaldelli, 2007-2[81](#_ENREF_81) | | 4 months | pioglitazone 45mg/day+SU | 10 | 55±4 | 50 | 28.9±1.3 | 6±2 | -2±0.6 | 9.3±0.4 | / | | / | |
| PBO+SU | 10 | 55±4 | 40 | 29.9±1.4 | 5±2 | 0.9±0.5 | 8.3±0.4 | / | | / | |
| Gram, 2011[42](#_ENREF_42) | | 2 years | PBO+NPH | 46 | 55.8±7.7 | 71.7 | 34.0±6.0 | 7.3±4.3 | -0.4±1.4 | 8.7±1.3 | 100.2±19.8 | | +5.3±20 | |
| metformin+NPH | 45 | 55.4±8.5 | 57.8 | 35.7±6.4 | 8.2±4.0 | -1.3±1.3 | 8.9±1.2 | 105.1±17.7 | | 2.9±20 | |
| rosiglitazone+NPH | 46 | 57.3±8.9 | 60.9 | 34.0±5.7 | 9.2±6.9 | -0.8±1.6 | 8.7±1.2 | 100.9±16.5 | | 7.6±20 | |
| metformin+rosiglitazone  +NPH | 46 | 57.3±8.2 | 65.2 | 34.4±7.0 | 8.1±5.3 | -1.7±1.1 | 8.5±1.1 | / | | / | |
| PBO+ASP | 48 | 57.1±8.5 | 47.9 | 33.7±5.0 | 9.1±5.5 | -0.6±1.2 | 8.5±1.2 | 98.3±16.6 | | 6.1±19 | |
| metformin+ASP | 45 | 56.1±8.2 | 62.2 | 33.7±6.1 | 8.7±4.5 | -1.2±1.2 | 8.5±1.2 | 100.5±17.9 | | 3.9±20 | |
| rosiglitazone+ASP | 47 | 56.1±8.3 | 57.4 | 32.7±4.7 | 9.4±6.3 | -1.2±1 | 8.3±1.0 | 95.6±14.6 | | 10.4±20 | |
| metformin+rosiglitazone  +ASP | 48 | 55.3±9.1 | 70.8 | 32.9±4.4 | 9.0±5.8 | -1.5±1.2 | 8.5±1.2 | / | | / | |
| Grey, 2012[118](#_ENREF_118) | | 6 months | pioglitazone 30mg daily | 10 | 61.9±10.0 | 60 | 31.2±4.7 | / | -0.28±0.3 | 7.6±2.1 | 90.1±14.9 | | / | |
| PBO | 10 | 57.9±15.2 | 50 | 33.2±4.1 | / | -0.04±0.4 | 7.1±1.0 | 91.7±12.8 | | / | |
| Henriksen, 2011[119](#_ENREF_119) | | 26 weeks | balaglitazone 10mg+insulin | 97 | 61.0±8.8 | 72 | 34.1±6.2 | 13.2±6.2 | -0.29±0.18 | 8.6±1.4 | / | | +3.5±1 | |
| balaglitazone 20mg+insulin | 97 | 60.5±9.0 | 55 | 34.1±5.5 | 14.7±7.4 | -0.41±0.19 | 8.5±1.1 | / | | +5±1 | |
| pioglitazone 45mg+insulin | 102 | 60.1±8.6 | 69 | 33.2±5.0 | 13.8±7.4 | -0.52±0.24 | 8.7±1.4 | / | | +4.9±1 | |
| PBO+insulin | 106 | 60.9±7.8 | 62 | 33.9±5.5 | 12.6±7.3 | 0.7±1.3 | 8.5±1.3 | / | | +0.5±1 | |
| Hollander, 2007[120](#_ENREF_120) | | 24 weeks | rosiglitazone 2mg/day+insulin | 193 | 52.7±9.6 | 57 | 32.8±7.4 | 12.5±8.3 | -0.6±1.1 | 8.9±1.1 | 97.2±22.3 | | +1.94±22.3 | |
| rosiglitazone 4mg/day+insulin | 189 | 52.6±10.1 | 48.1 | 33.7±7.1 | 13.0±7.3 | -0.8±1.2 | 9.0±1.2 | 96.8±20.8 | | +3.16±20.8 | |
| PBO+insulin | 186 | 53.8±10.2 | 46.2 | 33.0±6.5 | 12.6±8.6 | -0.3±1.3 | 9.1±1.3 | 95.1±20.9 | | +0.84±20.9 | |
| Iwamoto, 1996[121](#_ENREF_121) | | 12 weeks | Troglitazone 200mg bid+SU | 122 | 57.8±9.0 | 50.8 | 23.7±3.4 | / | -0.7±1.6 | 9.18±1.36 | 59.2±9.3 | | 0.6±1.3 | |
| PBO+SU | 126 | 58.7±8.0 | 42.9 | 23.3±3.1 | / | 0.2±1.7 | 8.98±1.45 | 57.7±9.6 | | -0.2±0.9 | |
| Kaku, 2009[122](#_ENREF_122) | | 28 weeks | Pioglitazone 30mg qd+metformin | 83 | 52±8.6 | 66.3 | 25.6±4.2 | 4.5±3.7 | -0.67±0.8 | 7.58±1.0 | / | | 1.68 | |
| PBO+metformin | 86 | 53±7.5 | 57 | 25.4±3.6 | 5.6±5.0 | 0.25±0.92 | 7.55±0.9 | / | | -0.47 | |
| Kawamori, 1998[123](#_ENREF_123) | | 12 weeks | pioglitazone 30mg Qd±SU | 21 | 57.6±8.5 | 66.7 | 23.0±1.8 | 12.5±9.1 | -0.8±1.4 | 8.4±1.4 | 61.1±6.6 | | +1.9±7.6 | |
| PBO±SU | 9 | 60.6±10.0 | 55.6 | 22.0±3.0 | 11.9±8.1 | -0.9±1.3 | 8.7±1.3 | 57.1±14.2 | | -1.1±14 | |
| Kelly, 1999[124](#_ENREF_124) | | 12 weeks | Troglitazone 200mg tid±SU | 11 | 58.0±8.6 | 72.7 | 28.7±3.9 | / | -0.84±0.7 | 7.51±1.38 | 78.9±11.2 | | 0.66±1.4 | |
| PBO±SU | 10 | 58.6±7.5 | 80 | 28.6±3.76 | / | 0.29±0.97 | 8.38±1.52 | 82.1±12.2 | | +0.25±0.9 | |
| Kipnes, 2001[125](#_ENREF_125) | | 16 weeks | pioglitazone 15mg Qd+SU | 184 | 56.5±9.8 | 59 | 31.4±5.0 | / | -0.8±0.2 | 10.0±0.2 | / | | / | |
| pioglitazone 30mg Qd+SU | 189 | 56.6±10.1 | 60 | 32.4±7.2 | / | -1.2±0.2 | 9.9±0.2 | / | | / | |
| PBO+SU | 187 | 56.9±8.9 | 58 | 32.0±4.9 | / | 0.1±0.2 | 9.9±0.2 | / | | / | |
| Marre, 2009[126](#_ENREF_126) | | 26 weeks | liraglutide 0.6mg+SU | 233 | 55.7±9.9 | 54 | 30.0±5.0 | 6.5 | -0.6±1 | 8.4±1.0 | 82.6±17.7 | | +0.7±17.7 | |
| liraglutide 1.2mg+SU | 228 | 57.7±9.0 | 45 | 29.8±5.1 | 6.7 | -1.08±1 | 8.5±1.1 | 80±17.1 | | +0.3±17.1 | |
| liraglutide 1.8mg+SU | 234 | 55.6±10.0 | 53 | 30.0±5.1 | 6.5 | -1.13±1 | 8.5±0.9 | 83±18.1 | | -0.2±18.1 | |
| PBO+SU | 114 | 54.7±10.0 | 47 | 30.3±5.4 | 6.5 | 0.23±1.0 | 8.4±1.0 | 81.9±17.1 | | -0.1±17.1 | |
| Rosiglitazone 4mg qd+SU | 232 | 56.0±9.8 | 47 | 29.4±4.8 | 6.6 | -0.44±1 | 8.4±1.0 | 80.6±17 | | +2.1±17 | |
| Mattoo, 2005[127](#_ENREF_127) | | 6 months | Pioglitazone 30mg qd+insulin | 142 | 58.8±7.4 | 43.7 | 32.5±4.8 | 13.6±6.8 | -0.69±0.09 | 8.85±0.11 | / | | 4.05±4.03 | |
| PBO+insulin | 147 | 58.9±6.9 | 42.9 | 31.8±5.0 | 13.4±6.1 | -0.13±0.1 | 8.79±0.10 | / | | 0.2±2.92 | |
| Mimura, 1994[128](#_ENREF_128) | | 3 months | CS 045 200mg bid | 8 | 53±2.7 | 50 | 22.4±0.7 | / | -2.5±0.4 | 9.3±0.4 | / | | / | |
| PBO | 6 | 58±2.1 | 50 | 21.3±1.4 | / | -0.4±0.3 | 9.7±0.3 | / | | / | |
| Negro, 2005[129](#_ENREF_129) | | 12 months | rosiglitazone 4mg bid+met | 19 | 60.3±6.4 | 52.6 | 28.3±1.7 | 7.1±2.4 | -1.1±0.7 | 8.4±0.6 | 84.1±4.6 | | +2.7±4.6 | |
| PBO+met | 19 | 59±8 | 63.2 | 28.7±1.9 | 6.6±2.9 | 0.2±0.5 | 8.1±0.5 | 83.6±4.4 | | 0.3±4.5 | |
| Osende, 2001[130](#_ENREF_130) | | 3 months | troglitazone 600mg Qd | 19 | 57.2±1.8 | 68.4 | 30.4±1.9 | / | -1.1±0.3 | 9.1±0.3 | / | | / | |
| PBO | 21 | 57.0±1.7 | 52.4 | 31.5±2.1 | / | -0.3±0.2 | 9.2±0.2 | / | | / | |
| Raskin, 2001[131](#_ENREF_131) | | 26 weeks | rosiglitazone 4mg/day+insulin | 106 | 57.7±10.2 | 56.6 | 32.1±4.8 | 12.7±7.3 | -0.6±1.1 | 9.1±1.3 | / | | / | |
| rosiglitazone 8mg/day+insulin | 103 | 57.1±10.0 | 54.4 | 32.3±4.9 | 12.5±8.0 | -1.2±1.1 | 9.0±1.3 | / | | / | |
| PBO+insulin | 104 | 55.6±10.3 | 55.8 | 32.7±6.2 | 11.7±6.2 | 0.1±1.0 | 8.9±1.1 | / | | / | |
|  | / | / | / | 36.3±1.8 | / | -1.3±0.5 | 9.8±0.5 | 106.4±6.4 | | -7.3±1.5 | |
| Rosenstock, 2008[132](#_ENREF_132) | | 26 weeks | rosiglitazone 4mg/day  +glimepide 3mg/day | 56 | 61±9 | 57 | 28.8±4.1 | 7.1±4.5 | -0.63±1.4 | 8.2±1.4 | 82.7±13.6 | | 0.9±13.6 | |
| rosiglitazone 8mg/day  +glimepide 3mg/day | 59 | 63±9 | 44 | 29.9±5.0 | 6.4±4.7 | -1.17±1.5 | 8.1±1.5 | 82.3±14.5 | | 1.7±14.5 | |
| PBO+glimepide 3mg/day | 57 | 65±9 | 60 | 29.1±4.5 | 6.6±3.9 | -0.08±1.3 | 7.9±1.3 | 83.1±14.2 | | -0.1±14.2 | |
| Schwartz, 1998[133](#_ENREF_133) | | 26 weeks | troglitazone 200mg/day+insulin | 116 | 56±9 | 47 | 34.8±6.3 | 10±5 | -0.8±1.1 | 9.5±1.1 | 98.4±20.5 | | 2.1±20.5 | |
| troglitazone 600mg/day+insulin | 116 | 56±9 | 46 | 35.1±5.5 | 10±5 | -1.4±1.1 | 9.3±1.1 | 100.7±17.9 | | 3.8±17.9 | |
| PBO+insulin | 118 | 56±10 | 51 | 35.0±6.3 | 10±4 | -0.1±1.1 | 9.4±1.1 | 100．6±19.3 | | 1.4±19.3 | |
| Smith, 2005[134](#_ENREF_134) | | 24 weeks | piogitazone 45mg/day | 21 | 56.2±9.7 | 42.9 | 32.1±5.6 | / | -0.96±1.11 | 6.88±1.35 | 93.5±19.6 | | 3.88±3.1 | |
| PBO | 21 | 53.1±9.3 | 47.6 | 31.9±5.0 | / | -0.11±0.79 | 6.46±0.72 | 91.5±14.9 | | -0.79±3.36 | |
| Scott, 2008[135](#_ENREF_135) | | 18 weeks | Sitagliptin+met | 94 | 55.2±9.8 | 55 | 30.3±4.7 | 4.9±3.5 | -0.73±0.13 | 7.8±1.0 | 83.1±17.1 | | -0.4±0.6 | |
| placebo+met | 92 | 55.3±9.3 | 59 | 30.0±4.5 | 5.4±3.7 | -0.22±0.14 | 7.7±0.9 | 84.6±16.5 | | -0.8±0.6 | |
| Rosiglitazone 8mg qd+met | 87 | 54.8±10.5 | 63 | 30.4±5.5 | 4.6±4 | -0.79±0.14 | 7.7±0.8 | 84.9±18.5 | | +1.5±0.45 | |
| Sridhar, 2013[136](#_ENREF_136) | | 24 weeks | pioglitazone 30mg/day  +glimepide+met | 25 | 47.9±5.8 | 100 | 25.3±2.7 | 2.2±1.7 | -0.4±0.4 | 6.8±0.4 | 70.4±11.4 | | +1.9±11.4 | |
| PBO+glimepide+met | 25 | 44.0±7.2 | 100 | 25.1±3.2 | 2.9±2.1 | -0.4±0.4 | 6.8±0.4 | 69.6±7.8 | | +0.3±7.8 | |
| Wolffenbuttel, 2000[137](#_ENREF_137) | | 26 weeks | rosiglitazone 1mg bid+SU | 199 | 61.0±9.4 | 62.8 | 28.0±3.9 | 7 | -0.59±1.2 | 9.20±1.19 | / | | / | |
| rosiglitazone 2mg bid+SU | 183 | 60.6±8.7 | 55.2 | 28.3±3.9 | 7 | -1.03±1.2 | 9.23±1.18 | / | | / | |
| PBO+SU | 192 | 61.9±9.1 | 57.3 | 28.1±4.1 | 8 | 0.25±1.3 | 9.21±1.30 | / | | / | |
| Yale, 2001[138](#_ENREF_138) | | 24 weeks | Troglitazone 400mg qd+metformin+SU | 101 | 58±0.9 | 55 | 30.1±0.5 | 11.9±0.8 | -1.4±0.2 | 9.6±0.1 | 85.2±1.6 | | +2.3±0.4 | |
| PBO+metformin+SU | 99 | 60±0.9 | 58 | 30.0±0.4 | 10.8±0.6 | 0.1±0.1 | 9.7±0.1 | 84.6±1.5 | | -0.1±0.4 | |
| Yang, 2002[139](#_ENREF_139) | | 6 months | Rosiglitazone 2mg bid+SU | 30 | 58.9±9.4 | 43.3 | 25.76±2.87 | / | -0.7±1 | 9.5±1.1 | 64.9±11.8 | | 3±2.4 | |
| PBO+SU | 34 | 57.8±8.9 | 38.2 | 25.84±3.50 | / | 0.4±1.3 | 9.7±1.4 | 65.3±11.2 | | -0.4±1.9 | |
| Zhu, 2003[140](#_ENREF_140) | | 24 weeks | rosiglitazone 2mg bid+SU | 215 | 59.0±7.5 | 41 | 24.8±3.4 | 7.2 | -1.4±0.15 | 9.9±1.6 | / | | / | |
| rosiglitazone 4mg bid+SU | 210 | 58.9±6.9 | 48 | 24.9±3.1 | 7.9 | -1.9±0.2 | 9.8±1.5 | / | | / | |
| PBO+SU | 105 | 58.8±7.7 | 46 | 25.1±2.8 | 7.6 | -0.4±0.25 | 9.8±1.3 | / | | / | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **DPP-IV inhibitor versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Aschner, 2006[141](#_ENREF_141) | | 24 weeks | placebo | 244 | 54.3±10.1 | 51.4 | 30.8±5.5 | 4.6±4.7 | 0.18±0.12 | 8.03±0.82 | / | | -1.1±0.2 | |
| Sitagliptin 100mg qd | 229 | 53.4±9.5 | 57.1 | 30.3±5.2 | 4.3±4.9 | -0.61±0.12 | 8.01±0.88 | / | | -0.2±0.2 | |
| Sitagliptin 200mg qd | 238 | 54.9±10.1 | 46.8 | 30.3±5.4 | 4.3±4.7 | -0.76±0.12 | 8.08±0.94 | / | | -0.1±0.2 | |
| Dejager, 2007[142](#_ENREF_142) | | 24 weeks | Vildagliptin 50mg qd | 104 | 55.3±11.4 | 41.3 | 32.9±6.0 | 2.1±3.6 | -0.8±0.1 | 8.2±0.8 | / | | -1.8±0.4 | |
| Vildagliptin 50mg bid | 90 | 52.8±9.6 | 46.7 | 33.3±4.8 | 2.1±3.3 | -0.85±0.1 | 8.6±0.8 | / | | -0.3±0.4 | |
| Vildagliptin 100mg qd | 92 | 53.6±10.8 | 53.3 | 32.4±6.1 | 2.4±4.2 | -0.9±0.1 | 8.4±0.8 | / | | -0.8±0.4 | |
| placebo | 94 | 52.2±11.2 | 47.9 | 32.6±5.6 | 1.6±2.5 | -0.3±0.1 | 8.4±0.8 | / | | -1.4±0.4 | |
| Frederich, 2012[143](#_ENREF_143) | | 24  weeks | Saxagliptin 2.5 mg q.A.M | 74 | 55.2±10.44 | 33.8 | 30.4±10.84 | 1.2±1.6 | -0.71±0.103 | 8.0±0.8 | 83.8±16.7 | | -0.3±0.35 | |
| Saxagliptin 5 mg q.A.M | 74 | 54.7±9.71 | 51.4 | 31.0±5.23 | 1.7±2.4 | -0.66±0.102 | 8.0±0.9 | 86.5±20.71 | | -0.9±0.31 | |
| Saxagliptin 2.5/5 mg q.A.M | 71 | 54.3±10.93 | 52.1 | 30.6±4.72 | 2.0±2.9 | -0.63±0.102 | 8.0±1.1 | 85.4±17.25 | | -0.9±0.41 | |
| Saxagliptin 5 mg q.P.M | 72 | 55.1±10.35 | 45.8 | 29.6±5.37 | 2.0±5.2 | -0.61±0.101 | 7.9±0.9 | 83.3±19.1 | | -0.4±0.36 | |
| Placebo | 74 | 55.6±10.32 | 47.3 | 31.1±4.54 | 1.7±2.8 | -0.26±0.103 | 7.8±1.0 | 85.4±14.4 | | -1.3±0.40 | |
| Goldstein, 2007[31](#_ENREF_31) | | 24 weeks | Sitagliptin 100mg qd | 175 | 53.3±10.2 | 52.0 | 31.2±5.9 | 4.4±4.6 | -0.66±0.165 | 8.87±0.99 | / | | / | |
| Metformin 500mg bid | 178 | 53.4±10.2 | 48.9 | 32.1±6.8 | 4.5±3.9 | -0.82±0.16 | 8.90±1.00 | / | | / | |
| Metformin 1000mg bid | 177 | 53.2±9.6 | 45.1 | 32.2±7.1 | 4.4±4.4 | -1.13±0.16 | 8.68±0.91 | / | | / | |
| placebo | 165 | 53.6±10.0 | 52.8 | 32.5±6.7 | 4.6±4.9 | 0.17±0.165 | 8.68±1.00 | / | | / | |
| Haak, 2012[33](#_ENREF_33) | | 24 weeks | Linagliptin 5 mg | 142 | 56.2±10.8 | 56.3 | 29.0±4.7 | / | -0.5±0.1 | 8.7±1.0 | 79.1±17.3 | | / | |
| Metformin 500mg bid | 141 | 52.9±10.4 | 56.9 | 28.9±4.8 | / | -0.6±0.1 | 8.7±0.9 | 79.9±18.4 | | / | |
| Metformin 1000mg bid | 138 | 55.2±10.6 | 53.1 | 29.5±5.3 | / | -1.1±0.1 | 8.5±0.9 | 80±18.5 | | / | |
| Placebo | 72 | 55.7±11.0 | 50 | 28.6±5.2 | / | 0.1±0.1 | 8.7±1.0 | 76.8±15.0 | | / | |
| Hanefeld, 2007[144](#_ENREF_144) | | 12  Weeks | Sitagliptin 25mg qd | 111 | 55.1±9.6 | 51.4 | 31.9±4.8 | 3.6±3.4. | -0.28±0.9 | 7.7±0.9 | / | / | |
| Sitagliptin 50mg qd | 112 | 55.3±10.3 | 45.5 | 31.6±4.9 | 3.3±3.9 | -0.44±1.0 | 7.6±1.0 | / | / | |
| Sitagliptin 100mg qd | 110 | 56.0±7.9 | 55.5 | 31.6±5.8 | 3.6±3.9 | -0.44±0.9 | 7.8±0.9 | / | / | |
| Sitagliptin 50mg bid | 111 | 55.2±9.5 | 44.1 | 32.7±4.8 | 4.5±5.9 | -0.43±0.9 | 7.8±0.9 | / | / | |
| placebo | 111 | 55.9±9.3 | 63.1 | 31.4±5.1 | 3.3±3.4 | 0.12±0.9 | 7.6±0.9 | / | / | |
| Inagaki, 2014[145](#_ENREF_145) | | 12  weeks | Placebo | 55 | 61.6±9.79 | 66 | 24.8±3.4 | 6.0±4.0 | 0·35±0·63 | 8·15±0·95 | / | | / | |
| SYR-472 12.5mg | 54 | 60.6±10.24 | 61 | 25.8±3.4 | 7.8±7.3 | –0·37±0·49 | 8·18±0·89 | / | | / | |
| SYR-472 25mg | 52 | 58.5±10.49 | 65 | 25.8±4.4 | 6.0±6.1 | –0·32±0·47 | 7·99±0·77 | / | | / | |
| SYR-472 50mg | 51 | 61.0±10.18 | 53 | 25.5±3.9 | 5.8±4.7 | –0·42±0·46 | 8·07±0·86 | / | | / | |
| SYR-472 100mg | 55 | 57.8±10.38 | 51 | 25.1±4.0 | 6.1±5.2 | –0·55±0·50 | 8·41±0·97 | / | | / | |
| SYR-472 200mg | 54 | 60.5±11.26 | 67 | 25.2±3.2 | 7.0±6.1 | –0·54±0·44 | 7·84±0·76 | / | | / | |
| Iwamoto, 2010[146](#_ENREF_146) | | 12 weeks | Placebo | 73 | 60.2±8.0 | 68.5 | 24.1±3.2 | 6.4±5.5 | 0.28±0.12 | 7.74±0.93 | / | | -0.5±0.35 | |
| Sitagliptin 25mg qd | 80 | 59.9±7.9 | 63.8 | 25.0±3.6 | 4.7±4.3 | / | 7.49±0.82 | / | | 0.4±0.3 | |
| Sitagliptin 50mg qd | 72 | 60.2±9.4 | 65.3 | 24.5±3.6 | 5.6±6.4 | / | 7.57±0.84 | / | | 0.3±0.3 | |
| Sitagliptin 100mg qd | 70 | 58.3±9.5 | 51.4 | 24.2±2.8 | 5.4±5.4 | -0.69±0.12 | 7.56±0.80 | / | | 0.1±0.35 | |
| Sitagliptin 200mg qd | 68 | 60.6±7.7 | 58.8 | 24.4±3.0 | 5.1±4.9 | / | 7.65±0.82 | / | | 0.4±0.3 | |
| Kawamori, 2012[147](#_ENREF_147) | | 12 weeks | Linagliptin 5 mg | 159 | 60.3±9.4 | 69.8 | 24.6 ±4.0 | / | -0.24±0.06 | 8.07 ±0.66 | / | | / | |
| Linagliptin 10 mg | 160 | 61.3±10.0 | 70.0 | 25.0 ±3.8 | / | -0.25±0.06 | 7.98±0.68 | / | | / | |
| Placebo | 80 | 59.7±8.9 | 71.3 | 24.3±3.4 | / | 0.63±0.08 | 7.95±0.67 | / | | / | |
| Kikuchi, 2009[148](#_ENREF_148) | | 12 weeks | vildagliptin 10 mg | 71 | 58.9±8. | 73.2 | 24.4 ±2.7 | 4.5 ±4.2 | -0.8±0.1 | 7.4 ±0.8 | 64.2±10.4 | | -0.2±5 | |
| vildagliptin 25 mg | 72 | 57.8 ±8.5 | 63.9 | 24.3 ±2.5 | 4.7 ±4.5 | -1.0±0.1 | 7.4±0.9 | 63.6±9.7 | | 0.2±1.3 | |
| vildagliptin 50 mg | 76 | 58.8 ±8.6 | 67.1 | 24.3 ±2.8 | 4.7±4.3 | -1.2±0.1 | 7.4 ±0.8 | 62.7±9.3 | | 0.5±1.4 | |
| Placebo | 72 | 60.4±8.1 | 63.9 | 24.6 ±3.1 | 7.1 ±5.5 | 0.2±0.1 | 7.4 ±0.8 | 63.8±10.1 | | -0.5±1.1 | |
| Mohan, 2009[149](#_ENREF_149) | | 18 weeks | Sitagliptin 100mg qd | 352 | 50.9 ± 9.3 | 57 | 25.1± 3.4 | 2.1± 1.7 | -0.7±0.1 | 8.7 ± 1.0 | 66.8±10.2 | | 0.6±0.1 | |
| Placebo | 178 | 50.9 ± 9.3 | 60 | 24.9 ± 3.4 | 1.9 ±1.6 | 0.3±0.2 | 8.8± 1.1 | 66.6±11.4 | | 0±0.2 | |
| Nonaka, 2008[150](#_ENREF_150) | | 12 weeks | Sitagliptin 100mg qd | 75 | 55.6±8.6 | 60 | 25.2±3.5 | 4.0±4.1 | -0.65±0.15 | 7.5±0.9 | / | | -0.1±0.35 | |
| Placebo | 76 | 55.0±8.0 | 66 | 25.1±3.2 | 4.1±4.6 | 0.41±0.15 | 7.7±0.9 | / | | -0.7±0.3 | |
| Del Prato, 2011[151](#_ENREF_151) | | 24 weeks | Linagliptin 5 mg | 333 | 56.4±10.1 | 48.8 | 29.04±4.80 | / | -0.44±0.05 | 8.0±0.05 | 78.53±16.73 | | / | |
| Placebo | 163 | 54.4±10.3 | 47.3 | 29.08±4.84 | / | 0.25±0.07 | 8.0±0.07 | 79.21±15.95 | | / | |
| Pan, 2012[152](#_ENREF_152) | | 24 weeks | Saxagliptin 5mg qd | 284 | 51.2 ±10.0 | 56.3 | 25.9 ±3.4 | 0.8 ±1.4 | -0.84±0.1 | 8.1 ±0.8 | 69.2±11.4 | | -0.32±11.4 | |
| Placebo | 284 | 51.6 ±10.3 | 54.6 | 25.9 ±3.7 | 1.2 ±2.6 | -0.34±0.1 | 8.2 ±0.8 | 69.2±12.4 | | -1.14±12.4 | |
| Pi-Sunyer, 2007[153](#_ENREF_153) | | 24 weeks | Vildagliptin 50mg qd | 88 | 50.6±10.4 | 55.7 | 31.9±5.4 | 1.8±2.7 | -0.5±0.1 | 8.4±0.9 | 90.5±22.3 | | -0.4±0.4 | |
| Vildagliptin 50mg bid | 83 | 50.2±12.7 | 56.6 | 32.2±6.0 | 2.4±3.2 | -0.75±0.1 | 8.4±0.9 | 89.9±18.5 | | 0±0.4 | |
| Vildagliptin 100mg qd | 91 | 52.0±11.7 | 53.8 | 31.9±5.0 | 2.1±2.9 | -0.8±0.1 | 8.3±0.8 | 90.8±19.9 | | -0.4±0.3 | |
| placebo | 92 | 52.0±12.0 | 54.3 | 32.7±6.4 | 2.5±3.7 | 0.0±0.1 | 8.5±0.8 | 93±23.2 | | -1.4±0.4 | |
| Raz, 2006[154](#_ENREF_154) | | 18 weeks | placebo | 103 | 55.5±10.1 | 62.7 | 32.5±5.2 | 4.7±5.0 | 0.12±0.17 | 8.05±0.9 | / | | -0.7±0.6 | |
| Sitagliptin 100mg qd | 193 | 54.5±10.0 | 53.7 | 31.8±5.3 | 4.5±4.3 | -0.48±0.13 | 8.04±0.82 | / | | -0.6±0.4 | |
| Sitagliptin 200mg qd | 199 | 55.4±9.2 | 50.5 | 32.0±5.3 | 4.5±3.9 | -0.36±0.12 | 8.14±0.91 | / | | -0.2±0.45 | |
| Ristic, 2005[155](#_ENREF_155) | | 12 weeks | Vildagliptin 25mg bid | 51 | 55.6±10.9 | 47.1 | 30.9±5.23 | 3.28±3.81 | -0.31±0.11 | 7.64±0.69 | 89.4±2.8 | | 0.06±0.33 | |
| Vildagliptin 25mg qd | 54 | 57.4±10.2 | 63 | 31.1±3.89 | 3.10±5.16 | -0.27±0.1 | 7.73±0.80 | 91.1±2 | | -0.55±0.32 | |
| Vildagliptin 50mg qd | 52 | 57.0±10.2 | 49.1 | 31.0±3.90 | 2.71±3.24 | -0.56±0.1 | 7.70±0.82 | 87.9±2.3 | | 0.04±0.33 | |
| Vildagliptin 100mg qd | 61 | 56.2±10.1 | 55.6 | 31.1±4.01 | 3.03±4.22 | -0.53±0.1 | 7.64±0.75 | 91.5±2.2 | | -0.07±0.31 | |
| Placebo | 55 | 54.6±10.6 | 56.9 | 31.6±4.41 | 2.28±2.99 | -0.13±0.1 | 7.76±0.83 | 92±2.1 | | -0.73±0.33 | |
| Roden, 2013[156](#_ENREF_156) | | 24  weeks | Placebo | 228 | 54.9±10.9 | 54 | 28.7±6.2 | / | 0.08±0.78 | 7.91±0.78 | 78.2±19.9 | | -0.33±0.33 | |
| Empagliflozin 10mg | 224 | 56.2±11.6 | 63 | 28.3±5.5 | / | -0.66±0.88 | 7.87±0.88 | 78.4±18.7 | | -2.26±0.35 | |
| Empagliflozin 25mg | 224 | 53.8±11.6 | 65 | 28.2±5.5 | / | -0.78±0.85 | 7.86±0.85 | 77.8±18.0 | | -2.48±0.35 | |
| Sitagliptin 100mg | 223 | 55.1±9.9 | 63 | 28.2±5.2 | / | -0.66±0.79 | 7.85±0.79 | 79.3±20.4 | | 0.18±0.34 | |
| Rosenstock, 2009[157](#_ENREF_157) | | 24 weeks | saxagliptin 2.5 mg | 102 | 53.27±10.06 | 56.9 | 31.90±4.82 | 3.1±3.5 | -0.43±0.1 | 7.9±0.9 | 92.1±18.39 | | -1.2±18.39 | |
| saxagliptin 5 mg | 106 | 53.91±11.57 | 50.9 | 32.24±4.5 | 2.5±3.3 | -0.46±0.1 | 8.0±1.1 | 90.87±18.15 | | -0.1±18.15 | |
| saxagliptin 10 mg | 98 | 52.72±11.27 | 45.9 | 31.71±4.71 | 2.3±3.1 | -0.54±0.1 | 7.8±0.9 | 89.3±17.67 | | -0.1±17.67 | |
| Placebo | 95 | 53.91±12.32 | 49.5 | 30.93±4.26 | 2.3±2.7 | 0.19±0.1 | 7.9±0.9 | 86.56±16.9 | | -1.4±16.9 | |
| Rosenstock, 2008[158](#_ENREF_158) | | 12 weeks | saxagliptin 2.5 mg | 55 | 52.5±10.53 | 40 | 30.8±3.73 | 1 | -0.72±0.12 | 7.7±0.97 | 86.6±14.17 | | -0.94±2.4 | |
| saxagliptin 5 mg | 47 | 53.7±10.14 | 53 | 30.8±4.21 | 0.8 | -0.9±0.14 | 7.9±1.09 | 89.8±15.92 | | -0.23±2.28 | |
| saxagliptin 10 mg | 63 | 54.5±8.61 | 63 | 31.0±4.03 | 0.7 | -0.81±0.11 | 8.0±1.14 | 92.4±17.78 | | -1.28±2.91 | |
| saxagliptin 20 mg | 54 | 53.6±8.59 | 70 | 29.7±3.63 | 1.7 | -0.74±0.12 | 7.9±0.99 | 88.9±14.63 | | -0.11±2.25 | |
| saxagliptin 40 mg | 52 | 54.1±11.12 | 58 | 29.8±4.29 | 1.3 | -0.80±0.12 | 7.8±1.00 | 86.8±19.55 | | 0.51±3.01 | |
| placebo | 67 | 55.2±9.8 | 63 | 31.1±4.46 | 1.8 | -0.27±0.11 | 8.0±0.88 | 93.1±19.21 | | -1.03±2.79 | |
| Scherbaum, 2008[159](#_ENREF_159) | | 52 weeks | Vildagliptin 50mg qd | 156 | 63.3±10.2 | 59.6 | 30.4±4.9 | 2.5±2.9 | -0.2±0.1 | 6.7±0.4 | / | | -0.5±0.3 | |
| placebo | 150 | 62.8±11.0 | 59.3 | 30.0±4.9 | 2.7±3.2 | 0.1±0.1 | 6.8±0.4 | / | | -0.2±0.3 | |
| Scott, 2007[10](#_ENREF_10) | | 12 weeks | Sitagliptin 5mg bid | 125 | 55.1±9.5 | 49.6 | 30.8±5.1 | 4.3±4.1 | -0.15±0.14 | 7.9±1.0 | / | | 0.1±1 | |
| Sitagliptin 12.5mg bid | 123 | 56.2±9.0 | 48 | 30.5±5.0 | 4.9±5.0 | -0.41±0.14 | 7.9±0.9 | / | | 0.1±1 | |
| Sitagliptin 25mg bid | 123 | 55.6±9.0 | 57.7 | 31.4±6.9 | 5.0±5.2 | -0.43±0.13 | 7.9±0.9 | / | | 0.3±1 | |
| Sitagliptin 50mg bid | 124 | 55.1±9.8 | 52.4 | 30.4±4.9 | 4.2±4.0 | -0.54±0.14 | 7.8±1.0 | / | | 0.4±1 | |
| placebo | 125 | 55.3±9.7 | 62.4 | 31.6±5.8 | 4.7±4.2 | 0.23±0.135 | 7.9±1.0 | / | | 0±1 | |
| Glipizide | 123 | 54.7±10.7 | 56.9 | 30.6±5.3 | 4.7±4.2 | -0.76±0.16 | 7.9±1 | / | | +0.9±1 | |
| Seino, 2011[160](#_ENREF_160) | | 12 weeks | Placebo | 75 | 59.1±10.47 | 74.7 | 24.39±3.69 | 6.83±6.07 | 0.06±0.456 | 7.85±0.89 | 64.57±12.01 | | -0.04±1.08 | |
| Alogliptin 6.25 mg | 79 | 58.1±10.58 | 70.9 | 24.75±4.85 | 6.63±6.41 | -0.51±0.677 | 7.85±0.94 | 65.5±14.47 | | 0.12±1.21 | |
| Alogliptin 12.5 mg | 84 | 58.7±9.54 | 70.2 | 24.86±4.04 | 5.94±5.32 | -0.70±0.572 | 7.99±0.88 | 67.21±13.41 | | 0.45±1.39 | |
| Alogliptin 25 mg | 80 | 59.5±11.16 | 78.8 | 24.70±4.15 | 6.98±6.99 | -0.76±0.547 | 7.88±0.99 | 66±13.34 | | 0.2±1.4 | |
| Alogliptin 50 mg | 79 | 58.8±9.23 | 69.6 | 24.29±3.02 | 6.78±5.95 | -0.82±0.474 | 8.01±0.97 | 63.8±10 | | 0.47±1.23 | |
| voglibose | 83 | 59.1±10.31 | 67.5 | 25.24±4.28 | 5.85±5.95 | -0.16±0.730 | 7.99±0.82 | 65.91±14.92 | | -0.46±1.62 | |
| **DPP-IV inhibitor versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Ahrén, 2004[161](#_ENREF_161) | | 12 weeks | LAF237 50mg qd+MET | 56 | 57.9 ± 10.0 | 69.6 | 29.4± 3.6 | 5.6 ± 4.2 | -0.7±0.1 | 7.7 ± 0.6 | / | | -0.4±0.2 | |
| Placebo+MET | 51 | 55.7 ± 11.0 | 66.7 | 30.2 ± 3.6 | 5.5± 3.7 | 0.1±0.1 | 7.8 ± 0.7 | / | | -0.5±0.2 | |
| Barnett, 2012[162](#_ENREF_162) | | 24 weeks | Saxagliptin 5mg qd+insulin±met | 304 | 57.2±9.43 | 40 | 32.6±5.65 | 11.8±6.93 | -0.73±0.054 | 8.7±0.9 | 87.7±18.57 | | 0.39±0.151 | |
| Placebo+insulin±met | 151 | 57.3±9.27 | 45 | 31.8±4.76 | 12.2±7.37 | -0.32±0.074 | 8.6±0.86 | 86.2±16.54 | | 0.18±0.209 | |
| Barnett, 2013[163](#_ENREF_163) | | 24  weeks | Linagliptin 5mg qd | 162 | 74.9±4.4 | 71.6 | 29.6±4.7 | / | -0.61±0.06 | 7.8±0.8 | 86.3±16.4 | | / | |
| Placebo | 79 | 74.9±4.2 | 62.0 | 29.8±4.5 | / | 0.04±0.07 | 7.7±0.7 | 84.4±15.3 | | / | |
| Bergenstal, 2012[164](#_ENREF_164) | | 24  weeks | Placebo+MET | 90 | 56.1±10.1 | 52 | 32.5±5.5 | 5.5±3.9 | -0.1±0.8 | 8.03±0.83 | 91.1±19.0 | | -0.5±19.0 | |
| Taspoglutide 10mg+MET | 182 | 55.3±9.5 | 56 | 32.7±5.2 | 6.1±4.8 | -1.23±0.06 | 7.95±0.93 | 93.6±20.4 | | -1.8±20.4 | |
| Taspoglutide 20mg+MET | 187 | 56.8±8.8 | 52 | 32.3±5 | 5.7±4.7 | -1.30±0.06 | 7.97±0.86 | 91.8±18 | | -2.6±18 | |
| Sitagliptin 100mg+MET | 177 | 55.5±9.9 | 59 | 32.4±5 | 6.0±5.0 | -0.89±0.06 | 7.94±0.85 | 92.5±19.7 | | -0.9±19.7 | |
| Bosi, 2007[165](#_ENREF_165) | | 24 weeks | vildagliptin50mg+MET | 143 | 54.3±9.7 | 57.3 | 32.1±5.3 | 6.8±5.5 | -0.9±0.1 | 8.4±0.9 | / | | -0.4±0.3 | |
| Vildagliptin100mg+MET | 143 | 53.9±9.5 | 61.5 | 32.9±5.0 | 5.8±4.7 | -0.5±0.1 | 8.4±1.0 | / | | 0.2±0.3 | |
| Placebo+MET | 130 | 54.5±10.3 | 53.1 | 33.2±6.1 | 6.2±5.3 | 0.2±0.1 | 8.3±0.9 | / | | -1±0.3 | |
| Bosi, 2011[166](#_ENREF_166) | | 52  weeks | Met+Pio30mg+Alogliptin25mg | 404 | 54.3±9.86 | 52.0 | 31.5±5.25 | 7.5±5.24 | -0.70±0.86 | 8.2±0.86 | 88.2±18.9 | | 1.1±0.194 | |
| Met+Pio45mg | 399 | 55.9±9.94 | 51.1 | 31.6±5.18 | 6.9±4.61 | -0.29±0.83 | 8.1±0.83 | 88±19.28 | | 1.6±0.194 | |
| Charbonnel, 2006[167](#_ENREF_167) | | 24 weeks | Sitagliptin 100mg qd+MET | 454 | 54.4±10.4 | 55.8 | 30.9±5.3 | 6.0±5.0 | -0.67±0.1 | 7.96±0.81 | / | | / | |
| Placebo+MET | 226 | 54.7±9.7 | 59.5 | 31.5±4.9 | 6.6±5.5 | -0.02±0.12 | 8.03±0.82 | / | | / | |
| DeFronzo, 2012[168](#_ENREF_168) | | 26 weeks | placebo+MET | 129 | 55.2±9.9 | 47.3 | 30.6±4.8 | 6.0±5.0 | -0.9±0.05 | 8.5±0.6 | / | | / | |
| Alogliptin 12.5mg+MET | 128 | 53.1±9.6 | 52.3 | 31.0±5.1 | 6.2±5.6 | / | 8.6±0.7 | / | | / | |
| Alogliptin 25mg+MET | 129 | 53.7±9.3 | 38.8 | 31.5±5.7 | 5.6±4.9 | -1.4±0.05 | 8.6±0.7 | / | | / | |
| Placebo+PIO 15mg+MET | 130 | 54.1±9.5 | 46.9 | 31.3±5.0 | 5.7±4.8 | -0.9±0.05 | 8.5±0.7 | / | | / | |
| Alogliptin 12.5mg  +PIO 15mg+MET | 130 | 53.6±9.9 | 46.2 | 31.5±5.0 | 6.1±5.5 | / | 8.5±0.7 | / | | / | |
| Alogliptin 25mg  +PIO 15mg+MET | 130 | 54.9±9.2 | 46.9 | 30.8±4.7 | 6.9±5.5 | / | 8.5±0.7 | / | | / | |
| Placebo+PIO 30mg+MET | 129 | 56.1±9.4 | 48.8 | 31.4±5.4 | 7.6±7.1 | -0.9±0.05 | 8.5±0.7 | / | | / | |
| Alogliptin 12.5mg  +PIO 30mg+MET | 130 | 55.0±9.1 | 41.5 | 31.1±5.1 | 5.8±5.1 | / | 8.5±0.7 | / | | / | |
| Alogliptin 25mg  +PIO 30mg+MET | 130 | 54.4±9.7 | 42.3 | 31.9±5.6 | 6.6±6.0 | / | 8.5±0.7 | / | | / | |
| Placebo+PIO 45mg+MET | 129 | 54.5±9.7 | 41.1 | 30.7±4.7 | 5.7±4.2 | -0.9±0.05 | 8.5±0.7 | / | | / | |
| Alogliptin 12.5mg  +PIO 45mg+MET | 130 | 54.0±9.8 | 46.2 | 31.5±5.2 | 6.6±5.3 | / | 8.5±0.7 | / | | / | |
| Alogliptin 25mg  +PIO 45mg+MET | 130 | 54.2±8.9 | 40 | 30.6±4.8 | 6.2±5.0 | -1.6±0.1 | 8.5±0.7 | / | | / | |
| Derosa, 2012[169](#_ENREF_169) | | 12 months | Sitagliptin 100mg qd+MET | 91 | 55.9±8.8 | 46 | 28.1±1.2 | 5.8±2.6 | -1.4±0.7 | 8.1±0.8 | 78.4±6.6 | | -2.5±5 | |
| Placebo+MET | 87 | 54.8±7.9 | 51 | 28.9±2.0 | 5.4±2.3 | -0.7±0.6 | 8.0±0.7 | 78.6±6.7 | | -2.3±5.2 | |
| Derosa, 2012[170](#_ENREF_170) | | 12 months | Vildagliptin 50mg bid+ metformin | 84 | 54.2±8.3 | 50 | 27.9±1.5 | 6.1±3.7 | -1.2±0.6 | 8.1±0.6 | 76.9±5.8 | | -5.8±3.6 | |
| Placebo+ metformin | 83 | 52.4±7.1 | 51.8 | 27.8±1.4 | 6.3±3.9 | -0.8±0.7 | 8.2±0.7 | 78.5±6.4 | | -5.1±4.3 | |
| Dobs, 2013[171](#_ENREF_171) | | 18 weeks | Sitagliptin 100mg qd+MET+rosi | 170 | 54.4±8.8 | 56 | 30.1±6.2 | 9.3±5.9 | -1.0±0.15 | 8.8±1.0 | 82.5±19.7 | | 1.8±0.3 | |
| Placebo+MET+rosi | 92 | 54.8±9.5 | 60 | 30.8±5.6 | 9.4±6.8 | -0.3±0.2 | 8.7±1.0 | 86.8±20 | | 1.2±0.5 | |
| Fonseca, 2007[172](#_ENREF_172) | | 24 weeks | Vildagliptin 50mg bid+insulin | 144 | 59.6±10.3 | 47.9 | 33.3±5.2 | 14.4±8.6 | -0.5±0.1 | 8.4±1.0 | / | | 1.3±0.3 | |
| Placebo+insulin | 152 | 58.9±10.8 | 54.6 | 32.9±5.9 | 14.9±8.4 | -0.2±0.1 | 8.4±1.1 | / | | 0.6±0.3 | |
| Fonseca, 2013[173](#_ENREF_173) | | 26  weeks | Sitagliptin100mg+MET+PIO | 157 | 55.7±8.7 | 61.8 | 29.9±5.2 | 9.4±5.8 | -1.1±0.15 | 8.8±1.0 | 82.1±19.1 | | 1.3±2.9 | |
| Placebo+MET+PIO | 156 | 56.4±9.4 | 62.8 | 30.0±5.2 | 10.2±6.1 | -0.4±0.1 | 8.7±1.0 | 83.8±19.1 | | 1.1±2.4 | |
| Forst, 2010[15](#_ENREF_15) | | 12 weeks | Linagliptin 1mg+met | 65 | 59.1±8.4 | 55.4 | 32.2±4.3 | 6.9±5.9 | -0.15±0.7 | 8.2±0.7 | 92.5±16.9 | | -0.15±16.9 | |
| Linagliptin 5mg+met | 66 | 59.6±9.8 | 56.1 | 31.7±4.5 | 7.3±7.5 | -0.5±0.81 | 8.5±0.8 | 90.7±14.2 | | -0.57±14.2 | |
| Linagliptin 10mg+met | 66 | 61.8±8.8 | 53 | 31.7±4.5 | 8.2±6.8 | -0.42±0.7 | 8.4±0.7 | 89.9±16.3 | | -1.27±16.3 | |
| Glimepiride+met | 65 | 59.4±9.9 | 63.1 | 31.5±4.2 | 6.7±5.9 | -0.68±0.7 | 8.2±0.7 | 90.5±15 | | +0.73±15 | |
| Placebo+met | 71 | 60.1±8.1 | 62 | 32.2±4.2 | 6.2±5.1 | 0.25±0.7 | 8.4±0.7 | 93.1±16.8 | | -0.84±16.8 | |
| Garber, 2007[174](#_ENREF_174) | | 24 weeks | Vildagliptin 50mg+PIO | 124 | 54.0±8.2 | 54.8 | 32.6±5.0 | 4.7±4.3 | -0.8±0.1 | 8.6±1.0 | / | | 0.1±0.4 | |
| Vildagliptin 100mg+PIO | 136 | 54.0±9.2 | 44.9 | 32.2±5.8 | 4.6±4.8 | -1±0.1 | 8.7±1.2 | / | | 1.3±0.4 | |
| placebo+PIO | 138 | 54.8±10.6 | 50.7 | 32.3±5.8 | 4.8±4.6 | -0.3±0.1 | 8.7±1.2 | / | | 1.4±0.3 | |
| Garber, 2008[175](#_ENREF_175) | | 24 weeks | Vildagliptin 50mg+SU | 132 | 58.6±10.6 | 59.1 | 32.2±4.9 | 6.9±5.2 | -0.58±0.10 | 8.5±0.9 | / | | -0.1±0.3 | |
| Vildagliptin 100mg+SU | 132 | 58.2±11.1 | 59.8 | 30.8±5.3 | 6.7±5.3 | -0.63±0.09 | 8.6±1.0 | / | | 1.3±0.3 | |
| placebo+SU | 144 | 57.9±10.5 | 58.3 | 31.0±5.5 | 7.8±5.8 | 0.07±0.09 | 8.5±1.0 | / | | -0.4±0.3 | |
| Gomis, 2011[176](#_ENREF_176) | | 24 weeks | Linagliptin 5mg+pio | 259 | 57.7±9.6 | 58.7 | 28.7±4.8 | / | -1.06±0.06 | 8.6±0.05 | 78.3±15.6 | | 2.3±15.6 | |
| Placebo+pio | 130 | 57.1±10.1 | 65.4 | 29.7±4.8 | / | -0.56±0.09 | 8.58±0.08 | 82.7±15.8 | | 1.2±15.8 | |
| Goodman, 2009[177](#_ENREF_177) | | 24 weeks | Vildagliptin 100mg qd+MET | 248 | 54.9±10.8 | 52.8 | 31.4±4.7 | / | -0.595±0.11 | 8.5±1 | / | | 0.06±1 | |
| placebo+MET | 122 | 54.5±9.7 | 67.2 | 31.7±4.3 | / | 0.17±0.11 | 8.7±1.1 | / | | -0.69±1 | |
| Haak, 2012[33](#_ENREF_33) | | 24 weeks | Placebo+Metformin 500 mg bid | 144 | 52.9±10.4 | 56.9 | 28.9±4.8 | / | -0.6±0.1 | 8.7±0.9 | 79.9±18.4 | | / | |
| Placebo+Metformin 1000 mg bid | 147 | 55.2±10.6 | 53.1 | 29.5±5.3 | / | -1.1±0.1 | 8.5±0.9 | 80±18.5 | | / | |
| LINA2.5mg+MET500mg | 143 | 55.6±11.2 | 51 | 29.7±5.3 | / | -1.2±0.1 | 8.7±1.0 | 80.8±19 | | / | |
| LINA2.5mg+MET 1000mg bid | 143 | 56.4±10.7 | 53.8 | 28.6±4.8 | / | -1.6±0.1 | 8.7±1.0 | 76.7±16 | | / | |
| Hermansen, 2007[178](#_ENREF_178) | | 24 weeks | Sitagliptin 100mg qd+Glimepiride±met | 222 | 55.6±9.6 | 52.7 | 31.2±6.3 | 8.3±5.5 | -0.45±0.12 | 8.34±0.76 | 86.5±21.1 | | 0.8±0.4 | |
| Placebo+ Glimepiride±met | 219 | 56.5±9.6 | 53.4 | 30.7±6.3 | 9.3±6.8 | 0.28±0.12 | 8.34±0.74 | 85.9±21.8 | | -0.4±0.45 | |
| Hollander, 2009[179](#_ENREF_179) | | 24 weeks | Saxagliptin 2.5mg+TZD | 195 | 54.9±9.7 | 54.4 | 30.0±5.8 | 5.3±4.6 | -0.66±0.06 | 8.3±1.1 | 82.1±22 | | 1.3±22 | |
| Saxagliptin 5mg+TZD | 186 | 53.2±10.6 | 47.8 | 29.8±5.3 | 5.2±5.6 | -0.94±0.06 | 8.4±1.1 | 80.4±19.4 | | 1.4±19.4 | |
| placebo+TZD | 184 | 54.0±10.1 | 46.2 | 30.3±5.8 | 5.1±5.4 | -0.3±0.06 | 8.2±1.1 | 80.9±21.5 | | 0.9±21.5 | |
| Jadzinsky, 2009[180](#_ENREF_180) | | 24 weeks | Saxagliptin 5mg+met | 320 | 52.0±10.4 | 51.6 | 29.9±4.5 | 2.0±3.6 | -2.5±0.1 | 9.4±1.2 | 82.1±16.3 | | -1.8±16.3 | |
| Saxagliptin 10mg+met | 323 | 52.1±11.6 | 45.2 | 30.3±5.0 | 1.4±2.5 | -2.5±0.1 | 9.5±1.2 | 82.5±16.9 | | -1.4±16.9 | |
| placebo+met | 328 | 51.8±10.7 | 49.7 | 30.2±4.9 | 1.7±3.1 | -2±0.1 | 9.4±1.3 | 82.8±17.5 | | -1.6±17.5 | |
| Kaku, 2011[181](#_ENREF_181) | | 12 weeks | Placebo + pioglitazone | 115 | 60.1 ±9.7 | 76/39 | 26.4 ±4.4 | 6.7 ±5.3 | -0.19±0.55 | 7.92 ±0.85 | 69±14.4 | | -0.03±1.52 | |
| Alogliptin 12.5 mg + pioglitazone | 111 | 60.8 ±8.8 | 67/44 | 25.91 ±4.7 | 6.51 ±5.0 | -0.91±0.44 | 7.91 ±0.82 | 66.5±12.9 | | 0.48±1.26 | |
| Alogliptin 25 mg + pioglitazone | 113 | 59.3 ±10.7 | 70/43 | 26.07 ±3.7 | 6.80 ±5.7 | -0.97±0.52 | 7.89 ±0.73 | 68.07±13 | | 0.46±1.42 | |
| Kadowaki, 2014[182](#_ENREF_182) | | 12  weeks | Placebo+glimepiride | 98 | 60.3±7.8 | 67.3 | 24.6±3.6 | 8.3±6.2 | 0.3±0.1 | 8.4±0.8 | 65.9±11.8 | | -0.2±0.1 | |
| Teneligliptin 20mg qd+glimepiride | 96 | 58.4±8.6 | 64.6 | 24.9±3.6 | 9.3±6.7 | −0.7±0.1 | 8.4±0.8 | 66.2±12.1 | | 0.4±0.1 | |
| Kikuchi, 2010[183](#_ENREF_183) | | 12  weeks | Vildagliptin 50mg bid+glimepiride | 102 | 59.2±9.8 | 73.5 | 24.5±2.9 | 8.6±6.7 | -1.0±0.06 | 7.8±0.8 | 65±0.95 | | 0.97±0.12 | |
| placebo+glimepiride | 100 | 60.3±10.1 | 69 | 24.4±2.6 | 9.8±6.4 | -0.06±0.06 | 8±0.8 | 63.6±0.96 | | 0.06±0.12 | |
| Kothny, 2012[184](#_ENREF_184) | | 52 weeks | Vildagliptin 50mg qd | 122 | 67.1±9.0 | 57.4 | 30.3±5.2 | / | -0.6±0.1 | 7.9±1.0 | / | | / | |
| Placebo | 89 | 69.3±7.2 | 61.8 | 30.1±5.0 | / | -0.2±0.2 | 7.9±1.0 | / | | / | |
| vildagliptin | 94 | 63.7±9.1 | 52.1 | 30.8±5.8 | / | -0.8±0.2 | 7.7±1.0 | / | | / | |
| Placebo | 64 | 65.4±10.5 | 51.6 | 30.0±4.7 | / | -0.1±0.2 | 7.5±1.1 | / | | / | |
| Lavalle-González, 2013[185](#_ENREF_185) | | 26  weeks | Placebo+met | 183 | 55.3±9.8 | 51.4 | 31.1±6.1 | 6.8±5.3 | –0.17±0.06 | 8.0±0.9 | 86.6±22.4 | | -1.0±0.3 | |
| Sitagliptin100mg+met | 366 | 55.3±9.8 | 47 | 32.0±6.1 | 6.8±5.2 | -0.82±0.04 | 7.9±0.9 | 87.7±21.6 | | -1.2±0.2 | |
| Canagliflozin100mg+met | 368 | 55.5±9.4 | 47.3 | 32.4±6.4 | 6.7±5.4 | -0.79±0.04 | 7.9±0.9 | 88.8±22.2 | | -3.3±0.2 | |
| Canagliflozin300mg+met | 367 | 55.4±9.4 | 45 | 31.4±6.3 | 7.1±5.4 | -0.94±0.04 | 7.9±0.9 | 85.4±20.9 | | -3.7±0.2 | |
| Lewin, 2012[186](#_ENREF_186)) | | 18 weeks | Linagliptin 5mg+SU | 161 | 57.2±9.8 | 47.8 | 28.4±5.0 | / | -0.54±0.07 | 8.6±0.9 | / | | / | |
| Placebo+SU | 84 | 56.2±10.2 | 61.9 | 28.2±5.1 | / | -0.07±0.1 | 8.6±0.7 | / | | / | |
| Lukashevic, 2014[187](#_ENREF_187) | | 24  weeks | Vildagliptin 50mg bid+Met+Glimepiride | 158 | 55.3±10.2 | 50.6 | 27.9±4.6 | 7.1±6.2 | -1.01±0.9 | 8.7±0.9 | 73.1 | | 0.5±1 | |
| Placebo+Met+Glimepiride | 160 | 55.0±11.1 | 45% | 28.0±4.5 | 7.5±6.1 | -0.25±0.9 | 8.8±0.9 | 72.4 | | -0.1±1 | |
| Nauck, 2009[188](#_ENREF_188) | | 26 weeks | Placebo+MET | 104 | 56±11 | 48 | 32±6 | 6±5 | -0.1±0.1 | 8.0±0.9 | / | | 0±0.7 | |
| Alogliptin 12.5mg+ MET | 213 | 55±11 | 47.4 | 32±5 | 6±5 | -0.6±0.1 | 7.9±0.7 | / | | 0±0.7 | |
| Alogliptin 25mg+ MET | 210 | 54±11 | 54.3 | 32±5 | 6±4 | -0.6±0.1 | 7.9±0.8 | / | | -0.3±0.7 | |
| Nowicki, 2011[189](#_ENREF_189) | | 12 weeks | Saxagliptin2.5mg qd +Insulin/OADs | 85 | 66.8±8.3 | 37.6 | 31.2±6.1 | 15.1±7.5 | -0.86±0.112 | 8.5±1.2 | 83.6±15.7 | | -0.5±15.7 | |
| placebo+Insulin/OADs | 85 | 66.2±9.1 | 48.2 | 30.2±6.8 | 18.2±8.5 | -0.44±0.109 | 8.1±1.1 | 82.2±14.4 | | 0±14.4 | |
| Owens, 2011[190](#_ENREF_190) | | 24 weeks | Linagliptin 5 mg+MET+SU | 792 | 58.3±9.9 | 46.8 | 28.4±4.8 | / | -0.72±0.03 | 8.15±0.03 | 76.5±16.8 | | / | |
| Placebo+MET+SU | 263 | 57.6±9.7 | 48.3 | 28.2±4.5 | / | -0.1±0.05 | 8.14±0.05 | 76.8±16.8 | | / | |
| Pan, 2012[191](#_ENREF_191) | | 24 weeks | Vildagliptin 50mg bid+ MET | 146 | 54.2±9.62 | 50 | 26.01±3.26 | 4.92±4.8 | -1.05±0.08 | 8.09±0.85 | 71.58±11.93 | | / | |
| Vildagliptin 50 mg qd+ MET | 146 | 53.7±10.0 | 44.6 | 25.03±3.09 | 5.02±4.42 | -0.92±0.08 | 8.05±0.84 | 68.36±11.1 | | / | |
| Placebo+MET | 144 | 54.5±9.68 | 45.8 | 25.46±3.09 | 5.15±4.58 | -0.54±0.08 | 8.01±0.82 | 69.83±11.18 | | / | |
| Pratley, 2009[192](#_ENREF_192) | | 24 weeks | Alogliptin 12.5mg+pio | 197 | 55.5±9.4 | 55.3 | 32.3±5.7 | / | -0.66±0.9 | 8.1±0.9 | / | | / | |
| Alogliptin 25mg+pio | 199 | 55.4±10.2 | 62.8 | 33.1±5.4 | / | -0.8±0.8 | 8.0±0.8 | / | | / | |
| Placebo+pio | 97 | 55.2±10.8 | 54.6 | 33.2±6.2 | / | -0.19±0.8 | 8.0±0.8 | / | | / | |
| Raz, 2008[193](#_ENREF_193) | | 18 weeks | Sitagliptin 100mg qd+met | 96 | 53.6±9.5 | 51 | 30.1±4.4 | 8.4±6.5 | -1±0.2 | 9.3±0.9 | 81.5±16.8 | | -0.5±16.8 | |
| placebo+met | 94 | 56.1±9.5 | 41.5 | 30.4±5.3 | 7.3±5.3 | 0±0.05 | 9.1±0.8 | 81.2±19.4 | | -0.5±19.4 | |
| Rosenstock, 2006[194](#_ENREF_194) | | 24 weeks | Sitagliptin 100mg qd+PIO | 175 | 55.6±10.4 | 53.1 | 32.0±5.2 | 6.1±5.4 | -0.85±0.13 | 8.1±0.8 | 90.9±17 | | 1.8±0.65 | |
| Placebo+PIO | 178 | 56.9±11.1 | 57.9 | 31.0±5.0 | 6.1±5.7 | -0.15±0.12 | 8.0±0.8 | 86.4±17.4 | | 1.5±0.65 | |
| Rosenstock, 2012[195](#_ENREF_195) | | 12 weeks | canagliflozin 50mg Qd+met | 64 | 53.3±8.5 | 53 | 31.7±4.6 | 5.6±5.0 | -0.57±0.99 | 8.00±0.99 | 87.6±16.3 | | -2.3±16.3 | |
| canagliflozin 100mg Qd+met | 64 | 51.7±8.0 | 56 | 31.7±5.0 | 6.1±4.7 | -0.54±0.96 | 7.83±0.96 | 87.7±15.5 | | -2.6±15.5 | |
| canagliflozin 200mg Qd+met | 65 | 52.9±9.6 | 51 | 31.4±5.2 | 6.4±5.7 | -0.48±0.80 | 7.61±0.80 | 87.7±17 | | -2.7±17 | |
| canagliflozin 300mg Qd+met | 64 | 52.3±6.9 | 56 | 31.6±4.9 | 5.9±5.2 | -0.70±1.02 | 7.69±1.02 | 87.3±15.9 | | -3.4±15.9 | |
| canagliflozin 300mg bid+met | 64 | 55.2±7.1 | 44 | 31.8±5.2 | 5.8±4.6 | -0.22±0.89 | 7.73±0.89 | 86±19.1 | | -3.4±19.1 | |
| sitagliptin 100mg Qd+met | 65 | 51.7±8.1 | 58 | 31.6±5.0 | 5.6±4.7 | -0.74±0.95 | 7.64±0.95 | 87.2±18 | | -0.6±18 | |
| PBO+met | 65 | 53.3±7.8 | 48 | 30.6±4.6 | 6.4±5.0 | -0.22±0.9 | 7.75±0.83 | 85.9±19.5 | | -1.1±19.5 | |
| Ross, 2012[196](#_ENREF_196) | | 12 weeks | Linagliptin 2.5mg+ metformin | 214 | 58.7±9.9 | 61.9 | 29.8±5.2 | / | -0.46±0.05 | 7.96±0.78 | 82.2±17.2 | | -0.4±4.8 | |
| Linagliptin 5mg+ metformin | 221 | 58.4±10.6 | 54 | 29.6±5.0 | / | -0.52±0.05 | 7.98±0.72 | 80.6±17.5 | | -1±2.2 | |
| Placebo+ metformin | 43 | 59.9±10.7 | 47.7 | 28.7±5.5 | / | 0.28±0.11 | 7.92±0.74 | 77.7±19.4 | | -1.1±1.9 | |
| Scott, 2008[135](#_ENREF_135) | | 18 weeks | Sitagliptin 100mg qd+met | 94 | 55.2±9.8 | 55 | 30.3±4.7 | 4.9±3.5 | -0.73±0.13 | 7.8±1.0 | 83.1±17.1 | | -0.4±0.6 | |
| placebo+met | 92 | 55.3±9.3 | 59 | 30.0±4.5 | 5.4±3.7 | -0.22±0.14 | 7.7±0.9 | 84.6±16.5 | | -0.8±0.6 | |
| Rosiglitazone+met | 87 | 54.8±10.5 | 63 | 30.4±5.5 | 4.6±4 | -0.79±0.14 | 7.7±0.8 | 84.9±18.5 | | +1.5±0.45 | |
| Seino, 2011[197](#_ENREF_197) | | 12 weeks | Placebo+voglibose | 75 | 62.3 ±10.5 | 48/27 | 24.42 ±4.20 | 7.52 ±6.03 | 0.04±0.46 | 8.12±1.19 | 64.4±10.5 | | -0.23±1.26 | |
| Alogliptin12.5 mg+voglibose | 76 | 61.0 ±10.1 | 44/32 | 24.36 ±4.08 | 7.28 ±5.13 | / | 8.02 ±0.99 | 62.8±13.2 | | 0.19±1.05 | |
| Alogliptin25 mg+voglibose | 79 | 62.9 ±9.0 | 50/29 | 23.26 ±2.88 | 8.44 ±5.90 | -0.91±0.48 | 7.91±0.91 | 60.4±10.0 | | -0.19±0.39 | |
| Seino, 2012[198](#_ENREF_198) | | 24 weeks | Alogliptin 12.5 mg od +metformin | 92 | 53.4 ±8.80 | 65.2 | 25.63 ±4.10 | 6.34 ±5.39 | -0.54±0.56 | 7.89 ±0.82 | 69.47±12.46 | | / | |
| Alogliptin 25 mg od +metformin | 96 | 52.3 ±8.02 | 68.8 | 25.79 ±3.70 | 6.62 ±4.80 | -0.64±0.49 | 8.02 ±0.73 | 69.65±12.67 | | / | |
| Placebo + metformin | 100 | 52.1 ±8.05 | 72 | 26.14 ±4.58 | 6.04 ±4.36 | 0.21±0.64 | 8.00 ±0.86 | 69.89±14.23 | | / | |
| Strain, 2013[199](#_ENREF_199) | | 24  weeks | Vildagliptin 50mg bid | 139 | 75.1±4.3 | 52.5 | 29.1±3.8 | 12.2±7.9 | -0.9±0.8 | 7.9±0.8 | 79.9±1 | | -0.1±1 | |
| placebo | 139 | 74.4±4 | 38.1 | 30.5±4.8 | 10.6±6.9 | -0.3±0.7 | 7.9±0.7 | 80.7±1 | | -1±1 | |
| Taskinen, 2011[200](#_ENREF_200) | | 24 weeks | Placebo+MET | 177 | 56.6±10.9 | 57 | 30.05±5.01 | / | 0.15±0.06 | 8.02±0.88 | 83.3±16.6 | | / | |
| Linagliptin 5mg qd+MET | 523 | 56.5±10.1 | 53 | 29.85±4.84 | / | -0.49±0.04 | 8.09±0.86 | 82.2±17.2 | | / | |
| Vilsbøll, 2010[201](#_ENREF_201) | | 24 weeks | Sitagliptin 100mg qd+insulin | 322 | 58.3±9.1 | 49 | 31±5 | 13±7 | -0.6±0.1 | 8.7±0.9 | 86.5±18.6 | | 0.1±0.3 | |
| placebo+insulin | 319 | 57.2±9.3 | 53 | 31±5 | 12±6 | 0.0±0.1 | 8.6±0.9 | 87.3±17.9 | | 0.1±0.35 | |
| Yang, 2011[202](#_ENREF_202) | | 24 weeks | Saxagliptin 5mg qd+MET | 283 | 53.8 ±10.4 | 48.1 | 26.3 ±3.6 | 5.1 ±5.0 | -0.78±0.1 | 7.9 ±0.8 | 68.9±12.5 | | / | |
| Placebo+MET | 287 | 54.4 ±10.1 | 48.7 | 26.1 ±3.5 | 5.1 ±4.0 | -0.37±0.1 | 7.9±0.8 | 69±11.9 | | / | |
| Yang, 2012[203](#_ENREF_203) | | 24 weeks | Sitagliptin 100mg qd+MET | 197 | 54.1±9.0 | 47 | 25.3±3.1 | 6.4±4.4 | -1.0±0.15 | 8.5±0.9 | 67.9±10.7 | | 0±0.35 | |
| Placebo+MET | 198 | 55.1±9.8 | 55 | 25.3±3.6 | 7.3±4.6 | -0.1±0.15 | 8.5±0.9 | 68.9±13.3 | | -0.5±0.4 | |
| Yang, 2015[204](#_ENREF_204) | | 24  weeks | Vildagliptin50mg qd+glimepiride | 143 | 58.3±9.8 | 55.2 | 24.8±3.0 | 6.9±4.6 | −0.7±0.1 | 8.6±0.9 | 67.4±11.1 | | -0.3±11.1 | |
| Placebo+glimepiride | 136 | 58.7±9.3 | 58.1 | 25.0±2.8 | 6.9±4.1 | −0.2±0.1 | 8.7±1.0 | 68.8±11.7 | | -0.6±11.7 | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **SGLT2 versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Bailey, 2012[205](#_ENREF_205) | | 24 weeks | dapagliflozin 1.0mg/day | 72 | 53.7±9.04 | 52.8 | 32.53±5.68 | 1.6±2.55 | -0.68±0.23 | 7.8±0.98 | 88.2±18.49 | | -2.69±0.75 | |
| dapagliflozin 2.5mg/day | 74 | 53.5±10.61 | 45.9 | 31.13±5.47 | 1.5±2.19 | -0.72±0.23 | 8.1±1.07 | 84.3±18.18 | | -2.64±0.7 | |
| dapagliflozin 5.0mg/day | 68 | 51.3±11.51 | 47.1 | 30.97±5.68 | 1.4±3.24 | -0.82±0.25 | 7.9±1.03 | 85.4±19.43 | | -2.69±0.7 | |
| PBO | 68 | 53.5±11.08 | 54.4 | 32.47±4.91 | 1.1±1.95 | 0.02±0.2 | 7.8±1.12 | 90±17.98 | | -0.96±0.8 | |
| Ferrannini, 2010[206](#_ENREF_206) | | 24 weeks | dapagliflozin 2.5mg morning | 65 | 53.0±11.7 | 55.4 | 32.6±5.5 | 0.5 | -0.58±0.11 | 7.92±0.90 | 90.8±22.8 | | -3.3±0.5 | |
| dapagliflozin 5.0mg morning | 64 | 52.6±10.9 | 48.4 | 31.9±4.8 | 0.25 | -0.77±0.11 | 7.86±0.94 | 87.6±17.1 | | -2.8±0.5 | |
| dapagliflozin 10.0mg morning | 70 | 50.6±9.97 | 48.6 | 33.6±5.4 | 0.45 | -0.89±0.11 | 8.01±0.96 | 94.2±18.7 | | -3.2±0.5 | |
| dapagliflozin 2.5mg evening | 67 | 54.3±11.5 | 43.3 | 32.2±5.3 | 0.2 | -0.83±0.11 | 7.99±0.99 | 88.3±20.5 | | -3.8±0.5 | |
| dapagliflozin 5.0mg evening | 68 | 54.5±11.0 | 42.6 | 32.8±5.3 | 0.5 | -0.79±0.11 | 7.82±0.91 | 89.2±20.5 | | -3.6±0.5 | |
| dapagliflozin 10.0mg evening | 76 | 50.7±9.7 | 51.3 | 33.3±5.6 | 0.4 | -0.79±0.10 | 7.99±1.05 | 92.1±22.0 | | -3.1±0.4 | |
| dapagliflozin 5.0mg morning | 34 | 48.3±9.3 | 70.6 | 32.6±4.6 | 0.65 | -2.88±1.41 | 10.82±0.93 | 88.7±19.2 | | -2.1±3.4 | |
| dapagliflozin 10.0mg morning | 39 | 47.9±12.1 | 59 | 31.1±5.9 | 1.4 | -2.66±1.26 | 10.73±0.85 | 87.5±22.7 | | -1.9±3.5 | |
| PBO | 75 | 52.7±10.3 | 41.3 | 32.3±5.5 | 0.5 | -0.23±0.1 | 7.84±0.87 | 88.8±19 | | -2.2±0.4 | |
| Ferrannini, 2013[207](#_ENREF_207) | | 12 weeks | empagliflozin 5mg/day | 81 | 59 | 56.8 | 28.5 | / | -0.4±0.15 | 7.9±0.8 | 82.8±50 | | -1.81±1.03 | |
| empagliflozin 10mg/day | 81 | 58 | 49.4 | 28.1 | / | -0.5±0.18 | 8.0±0.8 | 76.8±50 | | -2.33±1 | |
| empagliflozin 25mg/day | 82 | 57 | 50 | 28.3 | / | -0.6±0.15 | 7.8±0.8 | 81.2±40 | | -2.03±1 | |
| PBO | 82 | 58 | 54.9 | 28.8 | / | 0.1±0.18 | 7.8±0.8 | 82.2±50 | | -0.75±1 | |
| Fonseca, 2013[28](#_ENREF_28) | | 12 weeks | ipraliflozin 12.5mg Qd | 70 | 53.9±9.6 | 55.7 | 31.0±5.9 | 4.08±3.24 | -0.22±0.8 | 7.95±0.78 | 86±22.3 | | -1.5±0.75 | |
| ipraliflozin 50mg Qd | 67 | 52.6±10.7 | 50.7 | 32.2±5.9 | 4.61±4.65 | -0.39±0.8 | 8.05±0.81 | 90.7±20.8 | | -1.66±7.5 | |
| ipraliflozin 150mg Qd | 68 | 54.2±10.3 | 42.6 | 30.9±6.3 | 5.11±6.46 | -0.47±0.6 | 7.83±0.65 | 83.3±21.6 | | -2.08±7.5 | |
| ipraliflozin 300mg Qd | 68 | 54.2±10.7 | 54.4 | 30.7±5.0 | 4.48±4.91 | -0.55±0.6 | 7.90±0.67 | 86.7±19.6 | | -2.67±7.5 | |
| metformin | 69 | 53.1±11.7 | 58 | 29.8±5.5 | 4.13±4.71 | -0.46±0.9 | 8.03±0.90 | 84.1±21.8 | | -0.88±7.5 | |
| PBO | 69 | 53.4±9.7 | 46.4 | 30.9±5.5 | 4.64±5.93 | 0.26±0.78 | 7.84±0.78 | 81.8±17.4 | | -1±7.5 | |
| Inagaki, 2013[208](#_ENREF_208) | | 12  weeks | Placebo | 75 | 57.7±11.0 | 72.0 | 26.41±4.34 | / | 0.11±0.77 | 7.99±0.77 | 72.56±15.36 | | -0.78±15.36 | |
| Canagliflozin 50mg | 82 | 57.4±10.8 | 61.0 | 25.11±4.13 | / | -0.61±0.78 | 8.13±0.78 | 65.77±13.56 | | -1.98±13.56 | |
| Canagliflozin 100mg | 74 | 57.7±10.5 | 70.3 | 25.61±4.64 | / | -0.80±0.86 | 8.05±0.86 | 68.61±14.86 | | -2.51±14.86 | |
| Canagliflozin 200mg | 76 | 57.0±10.7 | 64.5 | 25.51±4.30 | / | -0.79±0.88 | 8.11±0.88 | 68.97±14.5 | | -2.39±14.5 | |
| Canagliflozin 300mg | 75 | 57.1±10.1 | 73.3 | 25.89±3.68 | / | -0.88±0.81 | 8.17±0.81 | 71.3±12.19 | | -3.19±12.19 | |
| Kaku, 2013[209](#_ENREF_209) | | 12 weeks | dapagliflozin 1mg | 59 | 55.9±9.7 | 79.7 | / | 4.89±4.37 | -0.12±0.07 | 8.10±0.79 | 68.4±11.04 | | -1.25±0.18 | |
| dapagliflozin 2.5mg | 56 | 57.7±9.3 | 69.6 | / | 4.41±3.97 | -0.11±0.07 | 7.92±0.74 | 66.61±14.29 | | -1.24±0.18 | |
| dapagliflozin 5mg | 58 | 58.0±9.5 | 81 | / | 5.34±4.51 | -0.37±0.07 | 8.05±0.66 | 68.92±12.43 | | -2.06±0.18 | |
| dapagliflozin 10mg | 52 | 56.5±11.5 | 75 | / | 4.73±4.73 | -0.37±0.07 | 8.18±0.69 | 70.35±17.48 | | -1.91±0.19 | |
| PBO | 54 | 58.4±10.0 | 79.6 | / | 4.74±3.82 | 0.37±0.07 | 8.12±0.71 | 68.88±14.94 | | -0.05±0.19 | |
| Ji, 2014[210](#_ENREF_210) | | 24  weeks | Placebo | 132 | 49.9±10.87 | 65.9 | 25.93±3.64 | 1.30±2.0 | -0.29±0.95 | 8.35±0.95 | 72.18±13.23 | | -0.27±0.45 | |
| Dapagliflozin 5mg | 128 | 53.0±11.07 | 65.6 | 25.17±3.29 | 1.15±2.3 | -1.04±0.74 | 8.14±0.74 | 68.89±11.43 | | -1.64±0.45 | |
| Dapagliflozin 10mg | 133 | 51.2±9.89 | 64.7 | 25.76±3.43 | 1.67±2.8 | -1.11±0.95 | 8.28±0.95 | 70.92±11.64 | | -2.25±0.15 | |
| List, 2009[36](#_ENREF_36) | | 12 weeks | dapagliflozin 2.5mg | 59 | 55±11 | 49 | 32±5 | / | -0.71±0.09 | 7.6±0.7 | 90±20 | | -2.7±0.75 | |
| dapagliflozin 5mg | 58 | 55±12 | 48 | 32±5 | / | -0.72±0.09 | 8.0±0.9 | 89±7 | | -2.5±0.75 | |
| dapagliflozin 10mg | 47 | 54±9 | 53 | 31±5 | / | -0.85±0.11 | 8.0±0.8 | 86±17 | | -2.7±0.85 | |
| dapagliflozin 20mg | 59 | 55±10 | 54 | 31±5 | / | -0.55±0.09 | 7.7±0.9 | 88±18 | | -3.4±0.75 | |
| dapagliflozin 50mg | 56 | 53±10 | 45 | 32±4 | / | -0.9±0.1 | 7.8±1.0 | 92±19 | | -3.4±0.75 | |
| PBO | 54 | 53±11 | 56 | 32±5 | / | -0.18±0.1 | 7.9±0.9 | 89±18 | | -1.2±0.75 | |
| metformin | 56 | 54±9 | 48 | 32±5 | / | -0.73±0.1 | 7.6±0.8 | 88±20 | | -1.7±0.75 | |
| Roden, 2013[156](#_ENREF_156) | | 24  weeks | Placebo | 228 | 54.9±10.9 | 54 | 28.7±6.2 | / | 0.08±0.78 | 7.91±0.78 | 78.2±19.9 | | -0.33±0.33 | |
| Empagliflozin 10mg | 224 | 56.2±11.6 | 63 | 28.3±5.5 | / | -0.66±0.88 | 7.87±0.88 | 78.4±18.7 | | -2.26±0.35 | |
| Empagliflozin 25mg | 224 | 53.8±11.6 | 65 | 28.2±5.5 | / | -0.78±0.85 | 7.86±0.85 | 77.8±18.0 | | -2.48±0.35 | |
| Sitagliptin 100mg | 223 | 55.1±9.9 | 63 | 28.2±5.2 | / | -0.66±0.79 | 7.85±0.79 | 79.3±20.4 | | 0.18±0.34 | |
| Stenlöf, 2013[211](#_ENREF_211) | | 26 weeks | canagliflozin 100mg/day | 195 | 55.1±10.8 | 41.5 | 31.3±6.6 | 4.5±4.4 | -0.77±1 | 8.1±1.0 | 85.8±21.4 | | -2.5±21.4 | |
| canagliflozin 300mg/day | 197 | 55.3±10.2 | 45.2 | 31.7±6.0 | 4.3±4.7 | -0.9±1 | 8.0±1.0 | 86.9±20.5 | | -3.4±20.5 | |
| PBO | 192 | 55.7±10.9 | 45.8 | 31.8±6.2 | 4.2±4.1 | 0.14±1.0 | 8.0±1.0 | 87.6±19.5 | | -0.5±19.5 | |
| **SGLT2 versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Bailey, 2010[212](#_ENREF_212) | | 24  weeks | Placebo+met | 137 | 53.7±10.3 | 55 | 31·8±5·3 | 5.8±5.1 | –0.30±0.96 | 8.11±0.96 | 87.7±19.2 | | -0.9±0.5 | |
| Dapagliozin 2·5 mg+met | 137 | 55.0±9.3 | 51 | 31·6±4·8 | 6.0±6.2 | –0.67±0.90 | 7.99±0.90 | 84.9±17.8 | | -2.2±0.5 | |
| Dapagliflozin 5 mg+met | 137 | 54.3±9.4 | 50 | 31·4±5·0 | 6·4±5.8 | –0.70±0.96 | 8.17±0.96 | 84.7±16.3 | | -3±0.5 | |
| Dapagliflozin 10 mg+met | 135 | 52·7±9.9 | 57 | 31·2±5·1 | 6.1±5.4 | –0.84±0.82 | 7.92±0.82 | 86.3±11.5 | | -2.9±0.5 | |
| Barnett, 2014[213](#_ENREF_213) | | 52  weeks | Placebo(CKD,2) | 95 | 62·6±8.1 | 58.9 | 30.8±5.6 | / | 0.06±0.80 | 8.09±0.80 | 88.4±0.45 | | -0.44±0.63 | |
| Empagliflozin10mg(CKD,2) | 98 | 63.2±8.5 | 61.2 | 32.4±5.4 | / | –0.57±0.84 | 8.02±0.84 | 86.97±0.45 | | -2±0.6 | |
| Empagliflozin25mg(CKD,2) | 97 | 62.0±8.4 | 62.9 | 31.3±5.8 | / | –0.60±0.73 | 7.96±0.73 | 86.4±0.45 | | -2.6±0.6 | |
| Placebo(CKD,3) | 187 | 65.1±8.2 | 56.7 | 30.3±5.3 | / | 0.12±0.80 | 8.09±0.80 | 82.85±0.35 | | 0±0.4 | |
| Empagliflozin25mg(CKD,3) | 187 | 64.6±8.9 | 57.2 | 30.2±5.3 | / | –0.32±0.84 | 8.02±0.84 | 81.68±0.5 | | -1.17±0.4 | |
| Placebo(CKD,4) | 37 | 62.9±11.9 | 51.4 | 31.8±6.0 | / | –0.37±0.99 | 8.16±0.99 | 84.1±21 | | 0±3.6 | |
| Empagliflozin25mg(CKD,4) | 37 | 65.4±10.2 | 56.8 | 29.0±4.9 | / | 0.11±1.05 | 8.06±1.05 | 76.5±15.9 | | -1±3.3 | |
| Bolinder, 2012[214](#_ENREF_214) | | 24  weeks | Placebo+metformin | 91 | 60.8±6.9 | 59.2 | 31.7±3.9 | 5.5±5.3 | -0.1±0.53 | 7.16±0.53 | 90.9±13.7 | | -0.8±13.7 | |
| Dapagliflozin 10mg qd+metformin | 89 | 60.6±8.2 | 58 | 32.1±3.9 | 6.0±4.5 | -0.39±0.44 | 7.19±0.44 | 92.1±14.1 | | -2.88±14.1 | |
| Forst, 2014[215](#_ENREF_215) | | 26  weeks | Placebo+MET+PIO | 115 | 58.3±9.6 | 66.1 | 32.5±6.4 | 10.1±6.6 | -0.26±1.0 | 8.0±1.0 | 93.8±22.4 | | -0.2±22.4 | |
| Canagliflozin100mg+MET+PIO | 113 | 56.7±10.4 | 68.1 | 32.3±6.2 | 10.5±6.6 | -1.89±0.9 | 8.0±0.9 | 94.2±22.2 | | -2.6±22.2 | |
| Canagliflozin300mg+MET+PIO | 114 | 57.0±10.2 | 55.3 | 32.8±7.7 | 11.0±7.6 | -1.03±0.9 | 7.9±0.9 | 94.4±25.9 | | -3.7±25.9 | |
| Häring  2013[216](#_ENREF_216) | | 24  weeks | Empagliflozin 10mg+MET+SU | 225 | 57.0±9.2 | 50 | 28.3±5.4 | / | -0.82±0.05 | 8.07±0.81 | 77.1±18.3 | | -2.16±18.3 | |
| Empagliflozin 25mg+MET+SU | 216 | 57.4±9.3 | 53 | 28.3±5.5 | / | -0.77±0.05 | 8.10±0.83 | 77.5±18.8 | | -2.39±18.8 | |
| Placebo+MET+SU | 225 | 56.9±9.2 | 50 | 27.9±4.9 | / | -0.17±0.05 | 8.15±0.83 | 76.2±16.9 | | -0.39±16.9 | |
| Häring, 2014[217](#_ENREF_217) | | 24  weeks | Placebo+MET | 207 | 56.0±9.7 | 56 | 28.7±5.2 | / | -0.13±0.05 | 7.90±0.88 | 79.7±18.6 | | -0.45±18.6 | |
| Empagliflozin 10mg+MET | 217 | 55.5±9.9 | 58 | 29.1±5.5 | / | -0.7±0.05 | 7.94±0.79 | 81.6±18.5 | | -2.08±18.5 | |
| Empagliflozin 25mg+MET | 213 | 55.6±10.2 | 56 | 29.7±5.7 | / | -0.77±0.05 | 7.86±0.87 | 82.2±19.3 | | -2.46±19.3 | |
| Henry, 2012[218](#_ENREF_218) | | 24 weeks | dapagliflozin 5mg/day+met | 194 | 51.7±9.3 | 40.2 | / | 1.6±2.4 | -2.05±0.17 | 9.2±1.3 | 84.1±19.5 | | -2.66±0.5 | |
| PBO+met | 201 | 51.8±9.8 | 47.3 | / | 1.6±2.6 | -1.35±0.17 | 9.2±1.3 | 85.6±20 | | -1.29±0.5 | |
| dapagliflozin 10mg/day+met | 211 | 51.0±10.1 | 50.2 | / | 2.2±3.3 | -1.98±0.15 | 9.1±1.3 | 88.4±19.7 | | -3.33±0.5 | |
| PBO+met | 208 | 52.7±10.4 | 46.6 | / | 1.9±4.0 | -1.44±0.14 | 9.1±1.3 | 87.2±19.4 | | -1.36±0.5 | |
| Kovacs, 2014[219](#_ENREF_219) | | 24  weeks | Placebo+pio+met | 165 | 54.6 ±10.5 | 44.2 | 29.3±5.4 | / | −0.11±0.07 | 8.2±0.92 | 78.1±20.1 | | 0.34±0.21 | |
| Empagliflozin 10mg+pio+met | 165 | 54.7±9.9 | 50.3 | 29.2±5.6 | / | −0.59±0.07 | 8.1±0.89 | 78±19.1 | | -1.62±0.21 | |
| Empagliflozin 25mg+pio+met | 168 | 54.2±8.9 | 50.6 | 29.1±5.5 | / | −0.72±0.07 | 8.1±0.82 | 78.9±19.9 | | -1.47±0.21 | |
| Lavalle-González, 2013[185](#_ENREF_185) | | 26  weeks | Placebo+met | 183 | 55.3±9.8 | 51.4 | 31.1±6.1 | 6.8±5.3 | –0.17±0.06 | 8.0±0.9 | 86.6±22.4 | | -1.0±0.3 | |
| Sitagliptin100mg+met | 366 | 55.3±9.8 | 47 | 32.0±6.1 | 6.8±5.2 | -0.82±0.04 | 7.9±0.9 | 87.7±21.6 | | -1.2±0.2 | |
| Canagliflozin100mg+met | 368 | 55.5±9.4 | 47.3 | 32.4±6.4 | 6.7±5.4 | -0.79±0.04 | 7.9±0.9 | 88.8±22.2 | | -3.3±0.2 | |
| Canagliflozin300mg+met | 367 | 55.4±9.4 | 45 | 31.4±6.3 | 7.1±5.4 | -0.94±0.04 | 7.9±0.9 | 85.4±20.9 | | -3.7±0.2 | |
| Ljunggren, 2012[220](#_ENREF_220) | | 50 weeks | dapagliflozin 10mg/day+met | 89 | 60.6±8.2 | 55.1 | 32.1±3.9 | 6.0±4.5 | -0.38±0.11 | 7.19±0.44 | 92.1±14.1 | | -4.39±0.85 | |
| PBO+met | 91 | 60.8±6.9 | 56 | 31.7±3.9 | 5.5±5.3 | 0.02±0.1 | 7.16±0.53 | 90.9±13.7 | | -2.03±0.88 | |
| Rosenstock, 2012[195](#_ENREF_195) | | 12 weeks | canagliflozin 50mg Qd+met | 64 | 53.3±8.5 | 53 | 31.7±4.6 | 5.6±5.0 | -0.57±0.99 | 8.00±0.99 | 87.6±16.3 | | -2.3±16.3 | |
| canagliflozin 100mg Qd+met | 64 | 51.7±8.0 | 56 | 31.7±5.0 | 6.1±4.7 | -0.54±0.96 | 7.83±0.96 | 87.7±15.5 | | -2.6±15.5 | |
| canagliflozin 200mg Qd+met | 65 | 52.9±9.6 | 51 | 31.4±5.2 | 6.4±5.7 | -0.48±0.80 | 7.61±0.80 | 87.7±17 | | -2.7±17 | |
| canagliflozin 300mg Qd+met | 64 | 52.3±6.9 | 56 | 31.6±4.9 | 5.9±5.2 | -0.70±1.02 | 7.69±1.02 | 87.3±15.9 | | -3.4±15.9 | |
| canagliflozin 300mg bid+met | 64 | 55.2±7.1 | 44 | 31.8±5.2 | 5.8±4.6 | -0.22±0.89 | 7.73±0.89 | 86±19.1 | | -3.4±19.1 | |
| sitagliptin 100mg Qd+met | 65 | 51.7±8.1 | 58 | 31.6±5.0 | 5.6±4.7 | -0.74±0.95 | 7.64±0.95 | 87.2±18 | | -0.6±18 | |
| PBO+met | 65 | 53.3±7.8 | 48 | 30.6±4.6 | 6.4±5.0 | -0.22±0.9 | 7.75±0.83 | 85.9±19.5 | | -1.1±19.5 | |
| Rosenstock, 2012[221](#_ENREF_221) | | 48 weeks | dapagliflozin 5mg/day+pio | 141 | 53.2±10.9 | 55.3 | / | 5.64±5.36 | -0.95±0.08 | 8.40±1.03 | 87.8±20.7 | | 1.35±0.38 | |
| dapagliflozin 10mg/day+pio | 140 | 53.8±10.4 | 42.1 | / | 5.75±6.44 | -1.21±0.07 | 8.37±0.96 | 84.8±22.2 | | 0.69±0.36 | |
| PBO+pio | 139 | 53.5±11.4 | 51.1 | / | 5.07±5.05 | -0.54±0.08 | 8.34±1.00 | 86.4±21.3 | | 2.99±0.41 | |
| Rosenstock, 2014[222](#_ENREF_222) | | 52  weeks | Insulin+Placebo | 188 | 55.3±10.1 | 40 | 34.7±4.3 | / | -0.81±0.08 | 8.33±0.72 | 96.66±1.72 | | 0.44±0.36 | |
| Insulin+Empagliflozin 10mg | 186 | 56.7±8.7 | 52 | 34.7±3.8 | / | -1.18±0.08 | 8.39±0.74 | 94.57±1.47 | | -1.95±0.36 | |
| Insulin+Empagliflozin 25mg | 189 | 58.0±9.4 | 44 | 35.0±4.0 | / | -1.27±0.08 | 8.29±0.72 | 93.41±1.72 | | -2.04±0.36 | |
| Strojek, 2011[223](#_ENREF_223) | | 24 weeks | dapagliflozin 2.5mg/day  +glimepiride 4mg/day | 154 | 59.9±10.14 | 50 | / | 7.7±6.0 | -0.58±0.5 | 8.11±0.75 | 81.89±0.6 | | -1.18±0.6 | |
| dapagliflozin 5.0mg/day  +glimepiride 4mg/day | 142 | 60.2±9.73 | 50 | / | 7.4±5.7 | -0.63±0.5 | 8.12±0.78 | 81±0.6 | | -1.56±0.6 | |
| dapagliflozin 10mg/day  +glimepiride 4mg/day | 151 | 58.9±8.32 | 43.7 | / | 7.2±5.5 | -0.82±0.7 | 8.07±0.79 | 80.56±0.65 | | -2.26±0.65 | |
| PBO+glimepiride 4mg/day | 145 | 60.3±10.16 | 49 | / | 7.4±5.7 | -0.13±0.7 | 8.15±0.74 | 80.94±1 | | -0.72±1 | |
| Wilding, 2009[224](#_ENREF_224) | | 12 weeks | dapagliflozin 10mg+insulin | 24 | 55.7±9.2 | 54.2 | 35.5±3.6 | 11.8±5.8 | -0.61±0.25 | 8.4±0.7 | 103.4±10.2 | | -4.5±1 | |
| dapagliflozin 20mg+insulin | 24 | 56.1±10.6 | 54.2 | 36.2±4.6 | 11.3±5.6 | -0.69±0.25 | 8.5±0.9 | 101.2±15.3 | | -4.3±1 | |
| PBO+insulin | 23 | 58.4±6.5 | 69.6 | 34.8±4.6 | 13.8±7.3 | 0.09±0.3 | 8.4±0.9 | 101.8±16.5 | | -1.9±1 | |
| Wilding, 2012[225](#_ENREF_225) | | 48 weeks | dapagliflozin 2.5mg+insulin | 202 | 59.8±7.6 | 49.5 | 33.0±5.0 | 13.6±6.6 | -0.79±0.78 | 8.46±0.78 | 93±16.7 | | -0.96±0.75 | |
| dapagliflozin 5mg+insulin | 211 | 59.3±7.9 | 47.4 | 33.0±5.3 | 13.1±7.8 | -0.96±0.89 | 8.62±0.89 | 93.3±17.4 | | -1±0.75 | |
| dapagliflozin 10mg+insulin | 194 | 59.3±8.8 | 44.8 | 33.4±5.1 | 14.2±7.3 | -1.01±0.82 | 8.57±0.82 | 94.5±16.8 | | -1.61±0.75 | |
| PBO+insulin | 193 | 58.8±8.6 | 49.2 | 33.1±5.9 | 13.5±7.3 | -0.47±0.77 | 8.47±0.77 | 94.5±19.8 | | +0.82±0.75 | |
| Wilding, 2013[226](#_ENREF_226) | | 12 weeks | ipragliflozin 12.5mg/day+met | 69 | 56.6±8.5 | 47.8 | 31.9±4.9 | 6.8±6.4 | -0.53±0.17 | 7.78±0.64 | 89.5±13.6 | | -0.92±0.63 | |
| ipragliflozin 50mg/day+met | 68 | 58.6±7.6 | 47.1 | 31.1±4.9 | 6.0±5.3 | -0.65±0.18 | 7.76±0.66 | 86.7±13.7 | | -2.1±0.65 | |
| ipragliflozin 150mg/day+met | 67 | 58.1±8.2 | 56.7 | 31.8±5.2 | 5.7±4.8 | -0.72±0.18 | 7.73±0.69 | 89.3±17 | | -1.99±0.65 | |
| ipragliflozin 300mg/day+met | 72 | 56.6±8.9 | 50 | 31.8±4.6 | 5.5±4.8 | -0.79±0.17 | 7.87±0.82 | 89.3±15 | | -2.21±0.66 | |
| PBO+met | 66 | 57.3±8.6 | 54.5 | 32.0±4.8 | 5.7±3.2 | -0.31±0.18 | 7.68±0.60 | 89±14.5 | | -0.48±0.5 | |
| Yale, 2013[227](#_ENREF_227) | | 26 weeks | canagliflozin 100mg/day | 90 | 69.5±8.2 | 64.4 | 32.4±5.5 | 15.6±7.4 | -0.3±0.9 | 7.9±0.9 | 90.5±18.4 | | 0.2±0.65 | |
| canagliflozin 300mg/day | 89 | 67.9±8.2 | 53.9 | 33.4±6.5 | 17.0±7.8 | -0.39±0.9 | 8.0±0.8 | 90.2±18.1 | | -1.2±0.65 | |
| PBO | 90 | 68.2±8.4 | 63.3 | 33.1±6.5 | 16.4±10.1 | -0.03±0.9 | 8.0±0.9 | 92.8±17.4 | | -1.4±0.65 | |
| **Author , year** | | **Study duration** | **Treatment group** | **No. of patients** | **Age (years)** | **Men (%)** | **BMI (kg/m2)** | **DM duration**  **(years)** | **HbA1c change (%)** | **Baseline HbA1c (%)** | **Baseline Weight**  **(kg)** | | **Weight Change**  **(kg)** | |
| **GLP-1 versus Placebo, monotherapy** | | | | | | | | | | |  | |  | |
| Fonseca, 2012[228](#_ENREF_228) | | 12 weeks | lixisenatide 2-step dose increase | 120 | 53.5±9.7 | 52.5 | 32.3±6.7 | 1.4 | -0.94±0.9 | 7.98±0.9 | 89±22 | | -2±20 | |
| lixisenatide 1-step dose increase | 119 | 53.8±10.9 | 52.9 | 31.7±6.6 | 1.1 | -0.77±0.9 | 8.07±0.9 | 86.5±21 | |
| PBO | 122 | 54.1±11.0 | 49.2 | 31.8±6.7 | 1.4 | -0.27±0.9 | 8.07±0.9 | 86.1±22 | |
| Madsbad, 2004[7](#_ENREF_7) | | 12 weeks | liraglutide 0.045mg Qd | 26 | 53±9.0 | 84.6 | 30.2±5.4 | 4.1±3.7 | 0.25±0.8 | 7.4±0.8 | / | | -0.03±0.96 | |
| liraglutide 0.225mg Qd | 24 | 58±7.5 | 62.5 | 32.0±5.3 | 4.4±4.0 | -0.34±0.8 | 7.9±0.8 | / | | -0.74±0.15 | |
| liraglutide 0.45mg Qd | 27 | 57±11.3 | 66.7 | 30.1±5.0 | 4.5±4.6 | -0.3±1 | 7.7±1.0 | / | | -1.2±0.02 | |
| liraglutide 0.60mg Qd | 30 | 57±7.7 | 66.7 | 30.4±4.8 | 4.6±4.6 | -0.7±1 | 7.4±1.2 | / | | 0.27±0.58 | |
| liraglutide 0.75mg Qd | 28 | 58±9.7 | 57.1 | 31.9±4.3 | 6.1±7.9 | -0.75±0.9 | 7.4±0.9 | / | | -0.39±0.44 | |
| PBO | 29 | 57±9.4 | 69 | 30.3±4.2 | 3.8±3.4 | -0.1±1.0 | 7.8±0.9 | / | | 0 | |
| glimepiride | 26 | 57±9.2 | 61.5 | 30.2±4.6 | 3.4±2.9 | -0.74±1.2 | 7.4±1.2 | / | | 0.94±0.02 | |
| Moretto, 2008[229](#_ENREF_229) | | 24 weeks | exenatide 5ug/day | 77 | 54±10 | 52 | 32±5 | 2±3 | -0.7±0.1 | 7.9±1.0 | 85±15 | | -2.8±0.3 | |
| exenatide 10ug/day | 78 | 55±10 | 62 | 31±5 | 2±3 | -0.9±0.1 | 7.8±1.0 | 86±16 | | -3.1±0.3 | |
| PBO | 77 | 53±9 | 55 | 32±5 | 1±2 | -0.2±0.1 | 7.8±0.9 | 86±16 | | -1.4±0.3 | |
| Rosenstock, 2009[230](#_ENREF_230) | | 16 weeks | exenatide 5-10ug bid | 34 | 53.7±9.4 | 45.7 | 32.4±5.1 | 6.4±5.4 | -0.54±0.91 | 8.0±0.9 | / | | -2.4±1 | |
| albiglutide 4mg weekly | 34 | 50.4±10.3 | 42.9 | 34.2±5.2 | 4.4±4.1 | -0.11±1.16 | 8.2±1.0 | / | | -1.1±1 | |
| albiglutide 15mg weekly | 34 | 55.5±10.5 | 51.4 | 31.1±4.1 | 4.7±4.6 | -0.49±0.74 | 8.0±0.9 | / | | / | |
| albiglutide 30mg weekly | 29 | 54.2±9.7 | 25.8 | 33.0±3.9 | 5.2±5.4 | -0.87±0.65 | 8.0±0.9 | / | | / | |
| albiglutide 15mg biweekly | 30 | 52.5±9.6 | 42.4 | 32.1±4.3 | 4.3±4.3 | -0.56±0.97 | 8.2±1.0 | / | | / | |
| albiglutide 30mg biweekly | 32 | 55.5±9.9 | 50.0 | 31.2±4.1 | 5.5±4.5 | -0.79±0.98 | 8.0±1.0 | / | | / | |
| albiglutide 50mg biweekly | 34 | 51.1±10.3 | 54.3 | 32.1±4.3 | 5.2±5.5 | -0.79±1.04 | 7.9±0.7 | / | | -1.7±1 | |
| albiglutide 50mg monthly | 35 | 54.1±11.1 | 48.6 | 31.6±4.9 | 5.3±3.7 | -0.55±1.01 | 7.9±0.8 | / | | / | |
| albiglutide 100mg monthly | 33 | 54.4±9.9 | 55.9 | 31.8±5.2 | 4.3±3.7 | -0.87±0.87 | 8.1±1.0 | / | | / | |
| PBO | 50 | 54.0±10.6 | 54.9 | 31.8±5.4 | 3.9±3.0 | -0.17±1.01 | 7.8±0.9 | / | | -0.7±1 | |
| Seino, 2008[231](#_ENREF_231) | | 14 weeks | liraglutide 0.1mg/day | 45 | 56.5±8.4 | 68.9 | 24.26±2.77 | 7.15±5.14 | -0.72±0.96 | 8.50±0.84 | 64.82±10.29 | | -0.05±0.68 | |
| liraglutide 0.3mg/day | 46 | 56.8±8.8 | 69.6 | 23.93±3.09 | 6.78±4.69 | -1.07±1.1 | 8.24±0.92 | 62.42±11.18 | | 0.13±0.68 | |
| liraglutide 0.6mg/day | 45 | 60.0±7.0 | 62.2 | 23.74±2.78 | 8.87±6.77 | -1.5±0.9 | 8.21±0.83 | 61.97±9.40 | | -0.1±0.68 | |
| liraglutide 0.9mg/day | 44 | 55.5±7.6 | 70.5 | 23.59±3.04 | 7.62±4.92 | -1.67±1.0 | 8.12±0.98 | 62.36±10.65 | | -0.48±0.68 | |
| PBO | 46 | 57.5±8.7 | 63 | 23.77±2.63 | 7.48±5.65 | 0.09±1.2 | 8.43±1.02 | 62.78±10.88 | | -0.95±0.68 | |
| Vilsbøll, 2007[232](#_ENREF_232) | | 14 weeks | liraglutide 0.65mg/day | 40 | 56.5±9.3 | 67.5 | 28.9±3.9 | 6 | -0.98±0.9 | 8.1±0.6 | / | | / | |
| liraglutide 1.25mg/day | 42 | 53.8±10.7 | 54.8 | 31.2±4.7 | 7 | -1.40±0.9 | 8.3±0.8 | / | | / | |
| liraglutide 1.9mg/day | 41 | 55.4±11.4 | 73.2 | 29.9±4.2 | 4 | -1.45±0.9 | 8.5±0.9 | / | | -2.99±1 | |
| PBO | 40 | 57.7±8.2 | 47.5 | 30.4±4.0 | 5 | +0.29±0.9 | 8.2±0.7 | / | | -1.78±1 | |
| Vilsbøll, 2008[233](#_ENREF_233) | | 14 weeks | liraglutide 0.65mg/day | 8 | 61.1±7.6 | 100 | 26.6±2.8 | 7.1±2.5 | -1.0±0.8 | 8.7±0.7 | 83.1±13.1 | | -1.3±2 | |
| liraglutide 1.25mg/day | 10 | 56.9±10.1 | 100 | 29.1±3.2 | 7.9±2.7 | -1.3±0.7 | 8.4±0.6 | 94.3±10.4 | | -2.4±2.4 | |
| liraglutide 1.9mg/day | 11 | 58.6±10.3 | 86 | 31.4±3.3 | 4.6±3.2 | -1.5±0.7 | 8.2±0.6 | 93.1±19.7 | | -2.8±2.7 | |
| PBO | 10 | 55.4±6.7 | 80 | 30.3±4.3 | 1.8±0.8 | 1.5±1.8 | 8.1±0.3 | 84.5±19.5 | | -4±4.8 | |
| **GLP-1 versus Placebo, add-on therapy** | | | | | | | | | | |  | |  | |
| Apovian, 2010[234](#_ENREF_234) | | 24 weeks | Exenatide 10ug bid+metformin | 52 | 53.4±10.7 | 29 | 32.9±3.5 | 4.3±3.2 | -0.9±0.8 | 7.5±0.8 | 91.4±13.2 | | -7.3±13.2 | |
| metformin+PBO | 51 | 55.0±7.9 | 39 | 33.6±4.6 | 3.9±3.2 | -0.4±0.5 | 7.2±0.5 | 94.9±14.3 | | -4.3±14.3 | |
| metformin+SU+exenatide10ug bid | 33 | 55.9±9.3 | 48 | 34.0±3.7 | 8.5±7.5 | -1.4±0.8 | 8.0±0.8 | 98.6±20.1 | | -5.2±20.1 | |
| metformin+SU+PBO | 36 | 55.1±9.9 | 31 | 34.3±4.0 | 7.6±6.9 | -0.9±0.9 | 7.9±0.9 | 96.5±17 | | -3.6±17 | |
| Exenatide 10ug bid+SU | 11 | 55.6±8.7 | 45 | 36.2±4.2 | 4.0±3.5 | -1.5±1.1 | 7.9±1.1 | 100.6±16.5 | | -4.2±16.5 | |
| SU+PBO | 11 | 55.3±11.3 | 54 | 33.8±4.3 | 4.3±2.8 | -1.3±1.1 | 7.7±1.1 | 100.8±17.4 | | -4.6±17.4 | |
| Bergenstal, 2012[164](#_ENREF_164) | | 24  weeks | Placebo+MET | 90 | 56.1±10.1 | 52 | 32.5±5.5 | 5.5±3.9 | -0.1±0.8 | 8.03±0.83 | 91.1±19.0 | | -0.5±19.0 | |
| Taspoglutide 10mg+MET | 182 | 55.3±9.5 | 56 | 32.7±5.2 | 6.1±4.8 | -1.23±0.8 | 7.95±0.93 | 93.6±20.4 | | -1.8±20.4 | |
| Taspoglutide 20mg+MET | 187 | 56.8±8.8 | 52 | 32.3±5 | 5.7±4.7 | -1.30±0.8 | 7.97±0.86 | 91.8±18 | | -2.6±18 | |
| Sitagliptin 100mg+MET | 177 | 55.5±9.9 | 59 | 32.4±5 | 6.0±5.0 | -0.89±0.8 | 7.94±0.85 | 92.5±19.7 | | -0.9±19.7 | |
| Buse, 2004[235](#_ENREF_235) | | 30 weeks | exenatide 5ug bid+SU | 125 | 55±10 | 59.2 | 33±6 | 6.3±5.2 | -0.46±0.12 | 8.5±1.1 | 95±22 | | -0.9±0.3 | |
| exenatide 10ug bid+SU | 129 | 56±11 | 57.4 | 33±6 | 6.6±6.6 | -0.86±0.11 | 8.6±1.2 | 95±18 | | -1.6±0.3 | |
| PBO+SU | 123 | 55±11 | 62.6 | 34±5 | 5.7±4.7 | 0.12±0.09 | 8.7±1.2 | 99±18 | | -0.6±0.3 | |
| Defronzo, 2005[236](#_ENREF_236) | | 30 weeks | exenatide 5ug bid+metformin | 110 | 55±11 | 51.8 | 34±6 | 6.2±5.9 | -0.4±0.11 | 8.3±1.1 | 100±22 | | -1.6±0.4 | |
| exenatide 10ug bid+metformin | 113 | 52±11 | 60.2 | 34±6 | 4.9±4.7 | -0.8±0.1 | 8.2±1.0 | 101±20 | | -2.8±0.5 | |
| PBO+metformin | 113 | 54±9 | 59.3 | 34±6 | 6.6±6.1 | 0.08±0.1 | 8.2±1.0 | 100±19 | | -0.3±0.3 | |
| Gao, 2009[237](#_ENREF_237) | | 12 weeks | Exenatide 10ug bid+met or met/SU | 234 | 55±9 | 48 | 26.4±3.2 | 8±6 | -1.2±0.1 | 8.3±1.0 | 69.6±11.2 | | -1.2±0.3 | |
| PBO+met or met/SU | 232 | 54±9 | 41 | 26.1±3.4 | 8±5 | -0.4±0.1 | 8.3±1.0 | 67.9±11.1 | | -0.1±0.25 | |
| Kadowaki, 2009[238](#_ENREF_238) | | 12 weeks | exenatide 2.5ug/day | 37 | 62.2±7.8 | 70.3 | 24.2±3.3 | 14.8±10.9 | -0.9±0.1 | 8.0±0.8 | 64.9±11.6 | | 0.08±0.2 | |
| exenatide 5ug/day | 37 | 60.7±9.8 | 67.6 | 25.0±3.4 | 11.3±6.4 | -1.2±0.1 | 7.9±0.8 | 65.6±9.8 | | -0.2±0.3 | |
| exenatide 10ug/day | 37 | 57.8±10.4 | 62.6 | 26.1±5.3 | 9.6±6.0 | -1.2±0.1 | 7.9±0.9 | 70.3±15.9 | | -1.3±0.3 | |
| PBO | 40 | 60.5±10.2 | 75 | 25.8±4.6 | 11.9±6.0 | 0.02±0.1 | 8.1±0.7 | 71.1±14 | | -0.7±0.2 | |
| Kaku, 2010[239](#_ENREF_239) | | 24 weeks | liraglutide 0.6mg/day+SU | 88 | 59.1±10.3 | 60 | 25.3±3.6 | 9.3±5.8 | -1.46±0.95 | 8.60±0.91 | 66.1±12.1 | | -1.12±0.55 | |
| liraglutide 0.9mg/day+SU | 88 | 61.3±11.0 | 67 | 24.4±3.4 | 11.6±7.7 | -1.56±0.84 | 8.21±0.78 | 64.5±12.0 | | -0.48±0.55 | |
| PBO+SU | 88 | 58.6±9.7 | 65 | 24.9±4.0 | 10.1±7.3 | -0.4±0.93 | 8.45±0.99 | 66.7±13.5 | | -0.37±0.55 | |
| Kendall, 2005[240](#_ENREF_240) | | 30 weeks | exenatide 5ug bid+met+SU | 245 | 55±9 | 59.2 | 33±6 | 8.7±5.9 | -0.7±0.1 | 8.5±1.0 | 97±19 | | -1.6±0.2 | |
| exenatide 10ug bid+met+SU | 241 | 55±10 | 59.3 | 34±6 | 8.7±6.4 | -0.6±0.1 | 8.5±1.1 | 98±21 | | -1.6±0.2 | |
| PBO+met+SU | 247 | 56±10 | 55.9 | 34±5 | 9.4±6.2 | 0.2±0.1 | 8.5±1.0 | 99±19 | | -0.9±0.2 | |
| Kim, 2007[241](#_ENREF_241) | | 15 weeks | exenatide LAR 0.8mg/day | 15 | 51±12 | 75 | 35±6 | 5±3 | -1.4±0.3 | 8.6±1.1 | 107±24 | | 0±1 | |
| exenatide LAR 2.0mg/day | 15 | 51±11 | 67 | 36±6 | 4±5 | -1.7±0.3 | 8.3±1.1 | 110±17 | | -3.8±1.4 | |
| PBO | 15 | 55±9 | 36 | 36±6 | 4±4 | 0.4±0.3 | 8.6±1.4 | 101±20 | | 0±1 | |
| Marre, 2009[126](#_ENREF_126) | | 26 weeks | liraglutide 0.6mg/day  +glimepiride 2-4mg/day | 233 | 55.7±9.9 | 54 | 30.0±5.0 | 6.5 | -0.6±1.0 | 8.4±1.0 | / | | / | |
| liraglutide 1.2mg/day  +glimepiride 2-4mg/day | 228 | 57.7±9.0 | 45 | 29.8±5.1 | 6.7 | -1.1±1.5 | 8.5±1.1 | / | | / | |
| liraglutide 1.8mg/day  +glimepiride 2-4mg/day | 234 | 55.6±10.0 | 53 | 30.0±5.1 | 6.5 | -1.1±1.1 | 8.5±0.9 | / | | / | |
| PBO+glimepiride 2-4mg/day | 114 | 54.7±10.0 | 47 | 30.3±5.4 | 6.5 | 0.2±1.0 | 8.4±1.0 | / | | / | |
| liraglutide 0.6mg/day  +rosiglitazone 4mg/day | 232 | 56.0±9.8 | 47 | 29.4±4.8 | 6.6 | -0.4±0.8 | 8.4±1.0 | / | | / | |
| Nauck, 2009[19](#_ENREF_19) | | 26 weeks | liraglutide 0.6mg/day+met | 242 | 56±11 | 62 | 30.5±4.8 | 7±5 | -0.7±0.1 | 8.4±0.9 | / | | / | |
| liraglutide 1.2mg/day+met | 240 | 57±9 | 54 | 31.1±4.8 | 7±5 | -1.0±0.1 | 8.3±1.0 | / | | / | |
| liraglutide 1.8mg/day+met | 242 | 57±9 | 59 | 30.9±4.6 | 8±5 | -1±0.1 | 8.4±1.0 | / | | / | |
| glimepiride 4mg/day+met | 242 | 57±9 | 57 | 31.2±4.6 | 8±5 | -1±0.1 | 8.4±1.0 | / | | / | |
| PBO+met | 121 | 56±9 | 60 | 31.6±4.4 | 8±6 | 0.1±0.1 | 8.4±1.1 | / | | / | |
| Ratner, 2010[242](#_ENREF_242) | | 13 weeks | lixisenatide 5ug Qd+met | 55 | 56.8±7.8 | 47.3 | 30.7±4.6 | 7.2±4.9 | -0.47±0.7 | 7.58±0.7 | 84.6±16 | | -2±0.4 | |
| lixisenatide 10ug Qd+met | 52 | 55.4±9.2 | 59.6 | 31.9±4.0 | 6.2±4.1 | -0.5±0.6 | 7.52±0.6 | 90.5±17 | | -2.39±0.42 | |
| lixisenatide 20ug Qd+met | 55 | 55.4±9.9 | 50.9 | 32.0±4.3 | 6.4±6.8 | -0.69±0.7 | 7.58±0.7 | 89.4±17 | | -3.01±0.41 | |
| lixisenatide 30ug Qd+met | 54 | 56.5±8.7 | 50 | 31.6±3.6 | 6.0±4.8 | -0.76±0.7 | 7.52±0.7 | 87.6±15 | | -3.47±0.41 | |
| lixisenatide 5ug bid+met | 53 | 57.1±8.2 | 47.2 | 31.6±4.2 | 6.2±6.0 | -0.65±0.6 | 7.60±0.6 | 86.5±14 | | -2.1±0.41 | |
| lixisenatide 10ug bid+met | 56 | 56.0±7.9 | 51.8 | 32.8±4.4 | 6.4±5.0 | -0.78±0.6 | 7.54±0.6 | 89.8±17 | | -2.21±0.41 | |
| lixisenatide 20ug bid+met | 54 | 56.7±8.3 | 37 | 32.7±4.4 | 6.6±5.1 | -0.75±0.7 | 7.61±0.7 | 88.5±17 | | -2.61±0.41 | |
| lixisenatide 30ug bid+met | 54 | 55.3±9.1 | 42.6 | 32.3±4.5 | 7.0±5.4 | -0.87±0.5 | 7.46±0.5 | 87.5±13 | | -3.89±0.41 | |
| PBO | 109 | 56.3±9.2 | 56 | 31.7±4.2 | 7.1±5.4 | -0.18±0.6 | 7.53±0.6 | 87.7±14 | | -1.94±0.32 | |
| Russell-Jones, 2009[243](#_ENREF_243) | | 26 weeks | Liraglutide 1.8mg qd+met+glimepide | 230 | 57.6±9.5 | 57 | 30.4±5.3 | 9.2±5.8 | -1.33±0.9 | 8.3±0.9 | 85.5±19.4 | | -1.8±0.33 | |
| PBO+met+glimepide | 114 | 57.5±9.6 | 49 | 31.3±5.0 | 9.4±6.2 | -0.24±0.9 | 8.3±0.9 | 85.7±16.7 | | -0.42±0.39 | |
| Umpierrez, 2011[244](#_ENREF_244) | | 16 weeks | LY 2189265 0.5/1.0mg | 66 | 59±12 | 53 | 33.7±4.1 | 9.0±7.6 | -1.32±0.12 | 8.25±0.9 | 94.8±17 | | -1.44±0.39 | |
| LY 2189265 1.0/1.0mg | 65 | 57±12 | 54 | 33.9±4.0 | 8.1±5.4 | -1.32±0.12 | 8.25±1.0 | 96.7±17 | | -1.34±0.39 | |
| LY 2189265 1.0/2.0mg | 65 | 54±11 | 52 | 34.2±4.1 | 8.6±6.9 | -1.59±0.12 | 8.43±1.0 | 98.6±18.4 | | -2.55±0.4 | |
| PBO | 66 | 56±12 | 44 | 33.9±4.3 | 7.5±5.4 | -0.3±0.8 | 8.05±0.8 | 94.7±15 | | -0.12±0.39 | |
| Zinman, 2007[245](#_ENREF_245) | | 16 weeks | Exenatide 10ug bid+TZD±metformin | 121 | 55.6±10.8 | 53.7 | 34.0±5.1 | 7.3±4.9 | -0.89±0.9 | 7.9±0.9 | 97.5±18.8 | | -1.75±0.65 | |
| PBO+TZD±metformin | 112 | 53.7±10.2 | 57.1 | 34.0±5.0 | 8.2±5.8 | 0.09±0.8 | 7.9±0.8 | 96.9±19.0 | | -0.24±0.65 | |
| Zinman, 2009[246](#_ENREF_246) | | 26 weeks | liraglutide 1.2mg/day+met 1g bid+RSG 4mg bid | 178 | 55±10 | 57 | 33.3±5.4 | 9±6 | -1.5±0.1 | 8.5±1.2 | / | | -1.0±0.3 | |
| liraglutide 1.8mg/day+met 1g bid+RSG 4mg bid | 178 | 55±11 | 51 | 33.5±5.1 | 9±6 | -1.5±0.1 | 8.6±1.2 | / | | -2±0.3 | |
| PBO+met 1g bid  +RSG 4mg bid | 177 | 55±10 | 62 | 33.9±5.2 | 9±6 | -0.5±0.1 | 8.4±1.2 | / | | 0.6±0.3 | |

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**Table S2: Meta-regression analysis for the relationship between baseline age and HbA1c changes in active hypoglycaemic agents compared with placebo\***

|  |  |  |  |
| --- | --- | --- | --- |
| Treatment | β | P | 95%CI |
| AGI | -0.145 | 0.178 | -0.359,0.069 |
| SU | 0.073 | 0.655 | -0.262,0.408 |
| MET | 0.298 | 0.481 | -0.567,1.164 |
| TZD | 0.140 | 0.225 | -0.089,0.369 |
| DPP4i | -0.007 | 0.949 | -0.221,0.207 |
| SGLT2i | 0.264 | 0.147 | -0.099,0.627 |
| GLP-1 | 0.307 | 0.448 | -0.517,1.132 |
| Total | 0.100 | 0.098 | -0.019,0.219 |

\*In the meta-regression analysis, the baseline age was used as the dependent variable, the HbA1c changes from baseline corrected by placebo was used as the independent factor, the baseline BMI, male percent, and baseline HbA1c were used as covariant.

**Table S3: Meta-regression analysis for the relationship between diagnosed age and HbA1c changes in active hypoglycaemic agents compared with placebo#**

|  |  |  |  |
| --- | --- | --- | --- |
| Treatment | β | P | 95%CI |
| AGI | -0.093 | 0.382 | -0.306,0.120 |
| SU | 0.063 | 0.716 | -0.297,0.423 |
| MET | -0.046 | 0.914 | -0.956,0.863 |
| TZD | 0.029 | 0.818 | -0.224,0.282 |
| DPP4i | 0.137 | 0.349 | -0.153,0.426 |
| SGLT2i | -0.071 | 0.836 | -0.786,0.643 |
| GLP-1 | 0.614 | 0.087 | -0.096,1.324 |
| Total | 0.072 | 0.298 | -0.064,0.209 |

# In the meta-regression analysis, the diagnosed age was used as the dependent variable, the HbA1c changes from baseline corrected by placebo was used as the independent factor, the baseline BMI, male percent, and baseline HbA1c were used as covariant.

**Table S4: PRISMA checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported on page #** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 4 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3,4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3,4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 3,4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 3,4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 3,4 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 4,5 |

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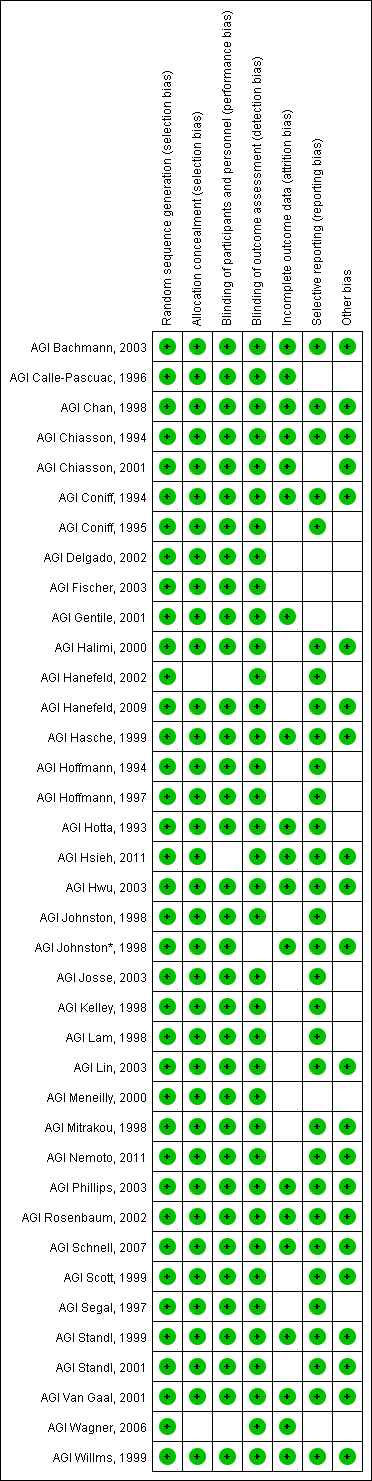
|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported on page #** |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 4,5 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 4,5 |
| **RESULTS** | | |  |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 5,6 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 5,6  supplement table S1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 6 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 6-9 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 6-9 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 8,9 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 6-9 supplement table S2 S3 |
| **DISCUSSION** | | |  |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 9-11 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 11 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 11 |
| **FUNDING** | | |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 11 |

*From:*  Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

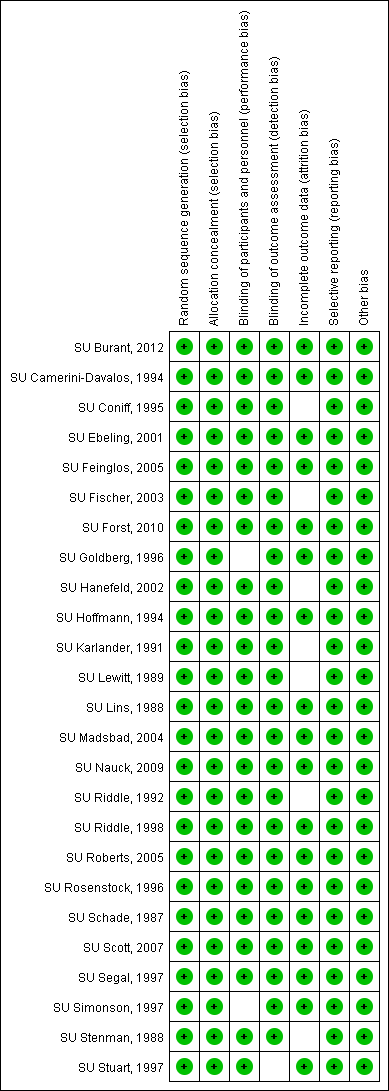
For more information, visit: **www.prisma-statement.org**.

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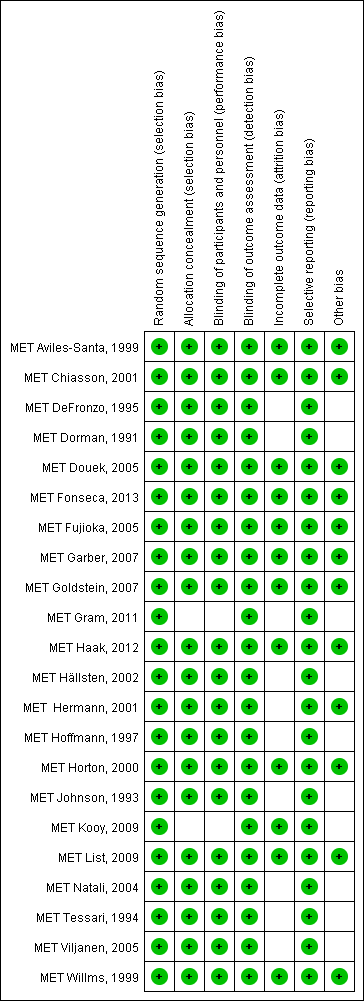
Supplement figure S1: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in AGI treatment.



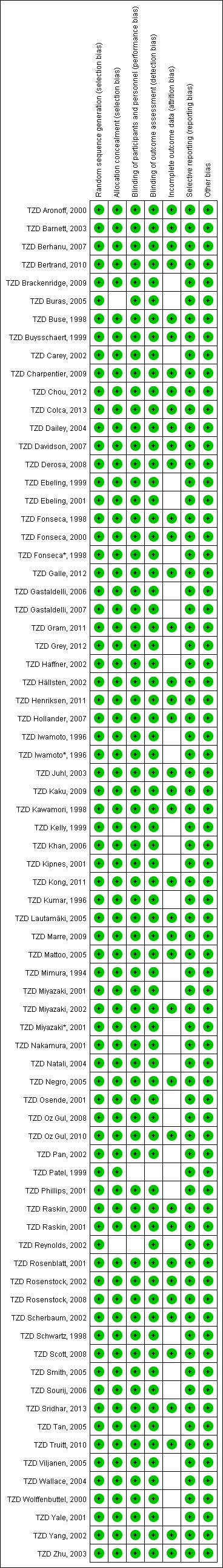
Supplement figure S2: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in SU treatment.



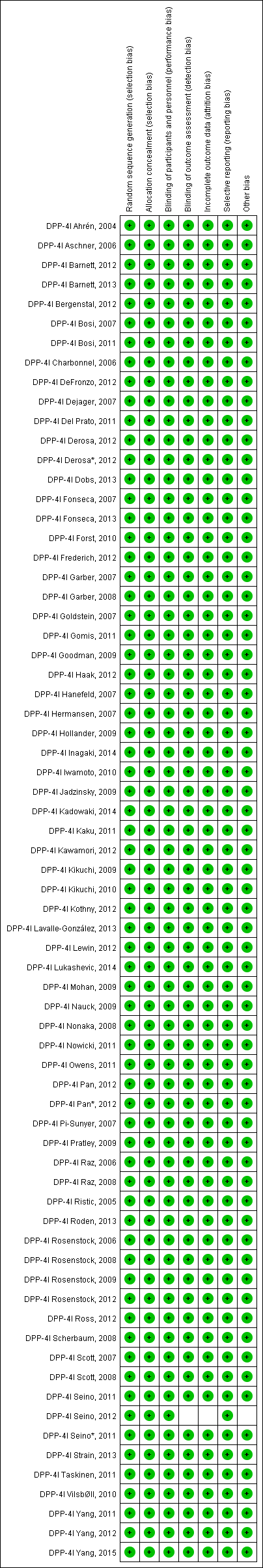
Supplement figure S3: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in MET treatment.



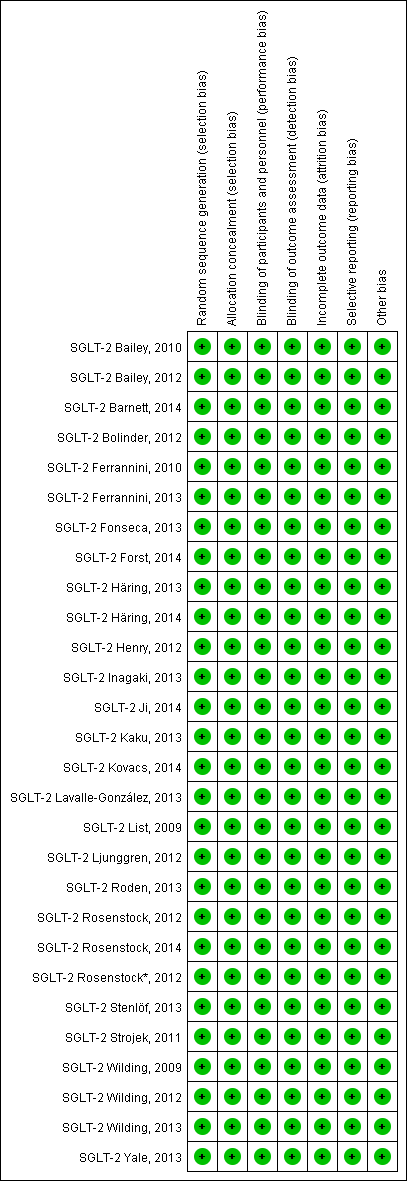
Supplement figure S4: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in TZD treatment.



Supplement figure S5: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in DPP-4i treatment.



Supplement figure S6: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in SGLT2i treatment.



Supplement figure S7: The quality of each study and the risk of bias were evaluated by the Cochrane instrument in GLP-1 treatment.

