

**Table S1. Baseline Characteristics of Randomized Controlled Trials Evaluating Antidiabetic Therapies in Addition to Metformin in Adults with Type 2 Diabetes**

Author, Year N <sup>a</sup>	Follow Up, weeks	Inclusion criteria	Interventions Evaluated <sup>b</sup>	Population Characteristics (Age, mean, years (SE); Males, %)	Baseline HbA <sub>1c</sub> , mean, % (SE)	SBP, mean, mmHg (SE)	Baseline weight, mean, kg (SE)	Baseline BMI, mean, kg/m <sup>2</sup> (SE)	Duration of DM, mean, years (SE)
Defronzo 2014 N=674	24	HbA <sub>1c</sub> : 7-10.5% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI: ≤45 kg/m <sup>2</sup> FPG: < 250 mg/dl	Empagliflozin 25 mg /Linagliptin 5 mg QD	Age: 57.1 (0.88) Males: 54%	7.9 (0.07)	130.9 (1.35)	85.5 (1.76)	NR	58.2% >5 years
			Empagliflozin 10 mg /Linagliptin 5 mg QD	Age: 56.2 (0.89) Males: 62%	8.0 (0.07)	130.5 (1.31)	86.6 (1.64)	NR	49.7% >5 years
			Empagliflozin 25 mg QD	Age: 55.5 (0.85) Males: 46%	8.0 (0.07)	129.2 (1.14)	87.7 (1.49)	NR	57.1% >5 years
			Empagliflozin 10 mg QD	Age: 56.1 (0.90) Males: 57%	8.0 (0.08)	131.6 (1.23)	86.1 (1.55)	NR	53.3% >5 years
			Linagliptin 5 mg QD	Age: 56.2 (0.88) Males: 50%	8.0 (0.08)	128.4 (1.11)	85.0 (1.62)	NR	57.8% >5 years
Bolli 2014 N=484	24	HbA <sub>1c</sub> : 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d FPG: < 250 mg/dl	Lixisenatide 20 µg, 1-step titration QD	Age: 55.4 (0.70) Males: 44%	8.0 (0.07)	NR	90.3 (1.50)	33.0 (0.46)	5.8 (0.31)
			Lixisenatide 20 µg, 2-step titration QD	Age: 54.6 (0.70) Males: 45%	8.1 (0.07)	NR	88.0 (1.32)	32.1 (0.38)	6.0 (0.36)
			Placebo	Age: 58.2 (0.77) Males: 45%	8.0 (0.06)	NR	87.9 (1.37)	32.4 (0.43)	6.2 (0.37)
Derosa 2014 N=167	26	HbA <sub>1c</sub> : 7-9% Metformin Dose: Maximum tolerated dose	Glimepiride 2 mg TID	Age: 57.2 (1.00) Males: 50%	7.7 (0.08)	NR	77.0 (0.70)	27.6 (0.14)	0.57 (0.03)
			Vildagliptin 50 mg BID	Age: 59.8 (1.07) Males: 49%	7.9 (0.10)	NR	77.8 (0.74)	27.9 (0.17)	0.58 (0.04)
Haring 2014 N=637	24	HbA <sub>1c</sub> : 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI: ≤45 kg/m <sup>2</sup>	Empagliflozin 10 mg QD	Age: 55.5 (0.67) Males: 58%	7.9 (0.05)	129.6 (0.96)	81.6 (1.26)	29.1 (0.37)	55% >5 years
			Empagliflozin 25 mg QD	Age: 55.6 (0.70) Males: 56%	7.9 (0.06)	130.0 (1.03)	82.2 (1.32)	29.7 (0.39)	59% >5 years
			Placebo	Age: 56.0 (0.67) Males: 56%	7.9 (0.06)	128.6 (1.02)	79.7 (1.29)	28.7 (0.36)	50% >5 years
Nauck 2014 N=1098	26	HbA <sub>1c</sub> : 7-9.5% ≥6 week lead-in for washout of other OADs and stabilize with metformin ≥1500 mg/d BMI: 25-40 kg/m <sup>2</sup> Weight: Stable for ≥12 weeks before screening	Sitagliptin 100 mg QD	Age: 54 (0.56) Males: 48%	8.1 (0.06)	127 (0.73)	86 (0.96)	31 (0.23)	7 (0.28)
			Placebo	Age: 55 (0.68) Males: 51%	8.1 (0.08)	128 (0.98)	87 (1.28)	31 (0.30)	7 (0.38)
Ridderstråle 2014 N=1549	52	HbA <sub>1c</sub> : 7-10% BMI: ≤45 kg/m <sup>2</sup> Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose)	Empagliflozin 25mg QD	Age: 56.2 (0.37) Males: 56%	7.9 (0.03)	133.4 (0.54)	82.5 (0.69)	30.0 (0.19)	45% >5 years
			Glimepiride 1-4mg QD	Age: 55.7 (0.37) Males: 54%	7.9 (0.03)	133.5 (0.57)	83.0 (0.69)	30.3 (0.19)	45% >5 years

<b>White 2014 N=160</b>	12	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d BMI: ≤45 kg/m <sup>2</sup>	Saxagliptin 2.5 mg BID	Age: 53.9 (1.20) Males: 54%	7.9 (0.11)	128.2 (1.76)	NR	33.7 (0.69)	5.8 (0.74)
			Placebo	Age: 56.6 (1.08) Males: 52%	8.0 (0.09)	127.4 (1.56)	NR	32.5 (0.67)	6.2 (0.45)
<b>Charbonnel 2013 N=653</b>	26	HbA1c: 7-11% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d FPG: <270 mg/dl	Sitagliptin 100 mg QD	Age: 56.9 (0.55) Males: 55%	8.2 (0.06)	130.0 (0.89)	91.0 (1.14)	32.6 (0.33)	7.6 (0.27)
			Liraglutide 1.2 mg QD	Age: 57.6 (0.60) Males: 55%	8.1 (0.05)	131.9 (0.90)	92.1 (1.13)	32.7 (0.34)	8.2 (0.34)
<b>Chawla 2013 N=52</b>	16	HbA1c: 7.5-11% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d FPG: ≥140 mg/dl	Sitagliptin 100 mg QD	Age: 49.5 (1.94) Males: 60%	8.1 (0.14)	NR	72.1 (2.76)	29.0 (0.99)	4.1 (0.74)
			Pioglitazone 30 mg QD	Age: 52.2 (1.90) Males: 56%	8.2 (0.16)	NR	72.7 (2.15)	28.7 (0.75)	4.5 (0.73)
<b>Cefalu 2013 N=1450</b>	52	HbA1c: 7.0-9.5% Stable therapy for ≥10 weeks Metformin ≥2000 mg/d (or 1500 mg/d if unable to tolerate a higher dose). If lower dose, then up to a 12 week dose-stable run-in period	Glimepiride 6 to 8 mg QD	Age: 56.3 (0.41) Males: 55%	7.8 (0.04)	129.5 (0.62)	86.5 (0.90)	30.9 (0.25)	6.6 (0.23)
			Canagliflozin 100 mg QD	Age: 56.4 (0.43) Males: 52%	7.8 (0.04)	130.0 (0.57)	86.9 (0.91)	31.0 (0.24)	6.5 (0.25)
			Canagliflozin 300 mg QD	Age: 55.8 (0.42) Males: 50%	7.8 (0.04)	130.0 (0.63)	86.6 (0.89)	31.2 (0.25)	6.7 (0.25)
<b>Derosa 2013 N=167</b>	52	HbA1c: >8.0% 35±8 week run-in of metformin 2500±500 mg/d BMI: 25-30 kg/m <sup>2</sup>	Vildagliptin 50 mg BID	Age: 54.2 (0.91) Males: 50%	8.1 (0.07)	NR	76.9 (0.63)	27.9 (0.16)	0.5 (0.03)
			Placebo	Age: 52.4 (0.78) Males: 52%	8.2 (0.08)	NR	78.5 (0.70)	27.8 (0.15)	0.5 (0.04)
<b>Lavalle-González 2013 N=1284</b>	26	HbA1c: 7-10.5% FPG: <15mmol/l Stable therapy for ≥8 weeks Metformin Dose: ≥2000 mg/d (≥1500 mg/d if unable to tolerate higher dose)	Canagliflozin 100 mg QD	Age: 55.5 (0.49) Males: 47%	7.9 (0.05)	128.0 (0.66)	88.8 (1.16)	32.4 (0.33)	6.7 (0.28)
			Canagliflozin 300 mg QD	Age: 55.3 (0.48) Males: 45%	7.9 (0.05)	128.7 (0.69)	85.4 (1.09)	31.4 (0.33)	7.1 (0.28)
			Sitagliptin 100 mg QD	Age: 55.5 (0.50) Males: 47%	7.9 (0.05)	128.0 (0.71)	87.7 (1.13)	32.0 (0.32)	6.8 (0.27)
			Placebo	Age: 55.3 (0.72) Males: 51%	8.0 (0.07)	128.0 (0.94)	86.6 (1.66)	31.1 (0.45)	6.8 (0.39)
<b>Rosenstock 2013 N=495</b>	12	HbA1c: 6.5-9% Stable therapy for ≥10 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) 4 week washout of other OADs BMI: ≤40 kg/m <sup>2</sup>	Empagliflozin 10 mg QD	Age: 59 (1.07) Males: 47%	7.9 (0.08)	132.4 (NR)	87.9 (1.71)	31.4 (0.47)	NR
			Empagliflozin 25 mg QD	Age: 59 (0.97) Males: 53%	8.1 (0.10)	135.3 (NR)	90.5 (2.02)	31.5 (0.57)	NR
			Sitagliptin 100 mg QD	Age: 58 (1.20) Males: 54%	8.1 (0.11)	135.5 (NR)	88.0 (1.78)	31.0 (0.53)	NR
			Placebo	Age: 60 (1.01) Males: 47%	8.0 (0.08)	136.0 (NR)	87.7 (1.86)	31.3 (0.53)	NR
<b>Rosenstock 2013 N=634</b>	24	HbA1c: 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d FPG: >250 mg/dl	Lixisenatide 20 µg, 2-step titration QD	Age: 57.3 (0.52) Males: 48%	8.0 (0.04)	NR	94.0 (1.10)	33.7 (0.35)	6.8 (0.31)
			Exenatide 10 µg BID	Age: 57.6 (0.60) Males: 59%	8.0 (0.05)	NR	96.1 (1.27)	33.5 (0.37)	6.8 (0.28)
<b>Aschner 2012 N=515</b>	24	HbA1c: 7-11% Stable therapy for ≥8 weeks Metformin Dose: ≥1000 mg/d BMI: 25-45 kg/m <sup>2</sup> FPG: <15.4 mmol/L	Insulin glargine titrated to FPG 4-5.5 mmol/L QD	Age 53.9 (0.59) Males: 50%	8.5 (0.07)	129.8 (0.88)	83.4 (1.21)	31.1 (0.33)	3.9 (NR)
			Sitagliptin 100 mg QD	Age: 53.3 (0.55) Males: 52%	8.5 (0.07)	131.7 (0.95)	84.2 (1.15)	31.3 (0.31)	4.8 (NR)

<b>Bergental 2012 N=666</b>	24	HbA1c: 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI: ≥25 kg/m <sup>2</sup> (or >23 kg/m <sup>2</sup> for Asian patients) Weight: Stable (<5% variance) for ≥12 weeks before screening	Sitagliptin 100 mg QD	Age: 55.5 (0.74) Males: 59%	8.0 (0.06)	NR	92.5 (1.48)	32.4 (0.38)	6.0 (0.38)
			Placebo	Age: 56.1 (1.06) Males: 52%	8.0 (0.09)	NR	91.1 (2.00)	32.5 (0.58)	5.5 (0.41)
<b>DeFronzo 2012 N=1554</b>	26	HbA1c: 7.5-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d If on 1000mg metformin, then titration to 1500mg for 2 weeks then optional 12 week stabilization BMI: 23-45 kg/m <sup>2</sup>	Placebo	Age: 55.2 (0.87) Males: 47%	8.5 (0.05)	NR	NR	30.6 (0.42)	6.0 (0.44)
			Alogliptin 12.5 mg QD	Age: 53.1 (0.85) Males: 52%	8.6 (0.06)	NR	NR	31 (0.45)	6.2 (0.49)
			Alogliptin 25 mg QD	Age: 53.7 (0.82) Males: 39%	8.6 (0.06)	NR	NR	31.5 (0.50)	5.6 (0.43)
			Pioglitazone 15 mg QD	Age: 54.1 (0.83) Males: 47%	8.5 (0.06)	NR	NR	31.3 (0.46)	5.7 (0.42)
			Pioglitazone 30 mg QD	Age: 56.1 (0.83) Males: 49%	8.5 (0.06)	NR	NR	31.4 (0.48)	7.6 (0.63)
			Pioglitazone 45 mg QD	Age: 54.5 (0.85) Males: 41%	8.5 (0.06)	NR	NR	30.7 (0.41)	5.7 (0.37)
			Alogliptin 12.5 mg + pioglitazone 15 mg QD	Age: 53.6 (0.87) Males: 46%	8.5 (0.06)	NR	NR	31.5 (0.44)	6.1 (0.48)
			Alogliptin 12.5 mg + pioglitazone 30 mg QD	Age: 55.0 (0.80) Males: 42%	8.5 (0.06)	NR	NR	31.1 (0.45)	5.8 (0.45)
			Alogliptin 12.5 mg + pioglitazone 45 mg QD	Age: 54.0 (0.86) Males: 46%	8.5 (0.06)	NR	NR	31.5 (0.46)	6.6 (0.46)
			Alogliptin 25 mg + pioglitazone 15 mg QD	Age: 54.9 (0.81) Males: 47%	8.5 (0.06)	NR	NR	30.8 (0.41)	6.9 (0.48)
			Alogliptin 25 mg + pioglitazone 30 mg QD	Age: 54.4 (0.85) Males: 42%	8.5 (0.06)	NR	NR	31.9 (0.49)	6.6 (0.53)
Alogliptin 25 mg + pioglitazone 45 mg QD	Age: 54.2 (0.78) Males: 40%	8.6 (0.06)	NR	NR	30.6 (0.42)	6.2 (0.44)			
<b>Derosa 2012 N=174</b>	52	HbA1c: 8-11% 8+/-2 month run-in period with 2500+/-500 mg/d BMI: 25-30 kg/m <sup>2</sup>	Exenatide 10 µg BID	Age: 57.3 (0.83) Males: 50%	8.1 (0.09)	NR	89.0 (1.05)	31.9 (0.18)	0.6 (0.02)
			Placebo	Age: 56.7 (0.79) Males: 48%	7.9 (0.07)	NR	90.5 (1.12)	31.7 (0.16)	0.7 (0.03)
<b>Derosa 2012 N=178</b>	52	HbA1c: >8% 8+/-2 month run-in period with 2500+/-500 mg/d BMI: 25-30 kg/m <sup>2</sup>	Sitagliptin 100 mg QD	Age: 55.9 (0.92) Males: 46%	8.1 (0.08)	NR	78.4 (0.69)	28.1 (0.13)	0.5 (0.02)
			Placebo	Age: 54.8 (0.85) Males: 51%	8.0 (0.08)	NR	78.6 (0.72)	28.9 (0.21)	0.5 (0.02)
<b>Gallwitz 2012 N=1029</b>	52	HbA1c: 6.5-9% Stable therapy for ≥12 weeks Metformin Dose: Max tolerated dose BMI: 25-40 kg/m <sup>2</sup>	Exenatide 10 µg BID	Age: 56 (0.45) Males: 56%	7.5 (0.03)	132.8 (0.71)	92.8 (0.75)	32.6 (0.19)	5.8 (0.22)
			Glimepiride, up to maximum tolerable dose	Age: 56 (0.41) Males: 52%	7.4 (0.03)	133.4 (0.68)	91.1 (0.67)	32.3 (0.18)	5.5 (0.19)

<b>Gallwitz 2012 N=1551</b>	52	HbA <sub>1c</sub> : 6.5-10% Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI: ≤40 kg/m <sup>2</sup> If on dual therapy, entered 6week washout period	Linagliptin 5 mg QD	Age: 59.8 (0.34) Males: 60%	7.7 (0.03)	NR	86.1 (0.63)	30.2 (0.17)	52 % >5 years
			Glimepiride 1-4 mg QD	Age: 59.8 (0.34) Males: 61%	7.7 (0.03)	NR	86.8 (0.60)	30.3 (0.17)	54% >5 years
<b>Ljunggren 2012 N=182</b>	50	HbA <sub>1c</sub> : 6.5-8.5% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d BMI: ≥25 kg/m <sup>2</sup> Weight: ≤120 kg FPG: ≤237.8 mg/dl	Dapagliflozin 10 mg QD	Age: 60.6 (0.87) Males: 55%	7.2 (0.06)	NR	92.1 (1.49)	32.1 (0.41)	6.0 (0.48)
			Placebo	Age: 60.8 (0.72) Males: 56%	7.2 (0.05)	NR	90.9 (1.44)	31.7 (0.41)	5.5 (0.56)
<b>Pan 2012 N=438</b>	24	HbA <sub>1c</sub> : 7-10% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d BMI: 20-40 kg/m <sup>2</sup> FPG: <270 mg/dl	Vildagliptin 50 mg QD	Age: 53.7 (0.82) Males: 55%	8.1 (0.07)	NR	68.4 (0.91)	25.0 (0.25)	5.0 (0.36)
			Vildagliptin 50 mg BID	Age: 54.2 (0.80) Males: 50%	8.1 (0.07)	NR	71.6 (0.99)	26.0 (0.27)	4.9 (0.40)
			Placebo	Age: 54.5 (0.81) Males: 56%	8.0 (0.07)	NR	69.8 (0.93)	25.5 (0.26)	5.2 (0.38)
<b>Rizzo 2012 N=90</b>	12	HbA <sub>1c</sub> : >7.5% Stable therapy for ≥8 weeks Metformin Dose: ≥2000 mg/d	Sitagliptin 100 mg QD	Age: 60 (1.27) Males: 44%	8.5 (0.16)	129 (2.24)	NR	30 (0.85)	8.6 (0.33)
			Vildagliptin 50 mg BID	Age: 60 (1.31) Males: 51%	8.2 (0.10)	132 (1.94)	NR	29.7 (0.76)	8.9 (0.28)
<b>Rosenstock 2012 N=451</b>	12	HbA <sub>1c</sub> : 7-10.5% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d BMI: 25-45 kg/m <sup>2</sup> (or 24-45 kg/m <sup>2</sup> for Asian patients) Weight: Stable	Placebo	Age: 53.3 (0.97) Males: 48%	7.8 (0.10)	125 (1.24)	85.9 (2.42)	30.6 (0.57)	6.4 (0.62)
			Canagliflozin 100 mg QD	Age: 51.7 (1.00) Males: 56%	7.8 (0.12)	127 (1.63)	87.7 (1.94)	31.7 (0.63)	6.1 (0.59)
			Canagliflozin 300 mg QD	Age: 52.3(0.86) Males: 56%	7.7 (0.13)	126 (1.50)	87.3 (1.99)	31.6 (0.61)	5.9 (0.65)
			Sitagliptin 100 mg QD	Age: 51.7 (1.00) Males: 59%	7.6 (0.12)	129 (1.61)	87.2 (2.23)	31.6 (0.62)	5.6 (0.58)
<b>Ross 2012 N=491</b>	12	HbA <sub>1c</sub> : 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI: ≤45 kg/m <sup>2</sup>	Linagliptin 2.5 mg BID	Age: 58.7 (0.66) Males: 62%	8.0 (0.05)	NR	82.2 (1.15)	29.8 (0.35)	52.3% >5 years
			Linagliptin 5 mg QD	Age: 58.4 (0.71) Males: 54%	8.0 (0.05)	NR	80.6 (1.17)	29.6 (0.33)	52.0% >5 years
			Placebo	Age: 59.9 (1.61) Males: 48%	7.9 (0.11)	NR	77.7 (2.92)	28.7 (0.83)	55.8% >5 years
<b>Arechavaleta 2011 N=1035</b>	30	HbA <sub>1c</sub> : 6.5-9% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d	Sitagliptin 100 mg QD	Age: 56.3 (0.43) Males: 55%	7.5 (0.03)	NR	80.6 (0.67)	29.7 (0.20)	6.8 (0.20)
			Glimeperide 1 – 6 mg QD	Age: 56.2 (0.44) Males: 54%	7.5 (0.04)	NR	82.0 (0.73)	30.2 (0.19)	6.7 (0.21)

<b>Nauck 2011 N=801</b>	52	HbA1c: 6.5-10% Therapy with mono- or dual OAD ≥8 weeks Metformin Dose: ≥1500 mg/d If taking <1500 mg/d then entered an 8week dose stabilization period with 1500-2000 mg/d FPG < 270.3 mg/dl	Dapagliflozin 2.5-10 mg QD	Age: 58 (0.45) Males: 55%	7.7 (0.05)	132.8 (NR)	96.4 (NR)	31.7 (0.26)	6 (0.25)
			Glipizide 5-20 mg QD	Age: 59 (0.50) Males: 55%	7.7 (0.05)	133.8 (NR)	96.5 (NR)	31.2 (0.25)	7 (0.30)
<b>Pfützner 2011 N=288</b>	24	HbA1c: ≥6.5-9% Stable therapy for ≥12 weeks Metformin Dose: Maximally tolerated dose (850-2000 mg)	Pioglitazone 15 mg BID	Age: 59 (0.83) Males: 66%	7.1 (0.05)	138 (1.24)	96.2 (1.45)	32.6 (0.41)	6.2 (0.45)
			Glimepiride 1 mg BID	Age: 59 (0.84) Males: 64%	7.4 (0.06)	137 (1.09)	94.1 (1.51)	32.5 (0.44)	5.9 (0.40)
<b>Taskinen 2011 N=700</b>	24	HbA1c: 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d (or maximum tolerated dose) BMI ≤40 kg/m <sup>2</sup>	Placebo	Age: 56.6 (0.82) Males: 57%	8.0 (0.07)	NR	83.3 (1.25)	30.1 (0.38)	53% >5 years
			Linagliptin 5 mg QD	Age: 56.5 (0.44) Males: 53%	8.1 (0.04)	NR	82.2 (0.75)	29.9 (0.21)	56% >5 years
<b>Wang 2011 N=55</b>	16	HbA1c: 7-11%; Therapy with mono- or dual OAD ≥12 weeks Metformin Dose: 1500 mg/d 8week monotherapy stabilization period	Acarbose 100 mg TID	Age: 52.8 (1.55) Males: 53.6%	8.2 (0.15)	129 (3.21)	69.8 (1.87)	25.9 (0.57)	7.6 (NR)
			Glibenclamide 5 mg TID	Age: 54.7 (1.73) Males: 44%	8.6 (0.33)	128 (3.34)	66.0 (3.21)	25.3 (0.79)	6.0 (NR)
<b>Yang 2011 N=570</b>	24	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d	Saxagliptin 5 mg QD	Age: 53.8 (0.62) Males: 48%	7.9 (0.05)	NR	68.9 (0.74)	26.3 (0.21)	5.1 (0.30)
			Placebo	Age: 54.4 (0.60) Males: 48%	7.9 (0.05)	NR	69.0 (0.70)	26.1 (0.21)	5.1 (0.24)
<b>Bailey 2010 N=546</b>	24	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d BMI: ≤45 kg/m <sup>2</sup>	Placebo	Age: 53.7 (0.88) Males: 55%	8.1 (0.08)	127.7 (1.25)	87.7 (1.64)	31.8 (0.45)	5.8 (0.44)
			Dapagliflozin 5 mg	Age: 54.3 (0.80) Males: 50%	8.2 (0.08)	126.9 (1.22)	84.7 (1.39)	31.4 (0.43)	6.4 (0.50)
			Dapagliflozin 10 mg QD	Age: 52.7 (0.85) Males: 57%	7.9 (0.07)	126.0 (1.37)	86.3 (1.50)	31.2 (0.44)	6.1 (0.46)
<b>Filozof 2010 N=1007</b>	52	HbA1c: 7.5-11% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d	Vildagliptin 50 mg BID	Age: 59.2 (0.44) Males: 52%	8.5 (0.04)	NR	85.7 (0.73)	31.2 (0.22)	6.4 (0.23)
			Gliclazide 80-320 mg QD	Age: 59.7 (0.46) Males: 52%	8.5 (0.04)	NR	84.2 (0.81)	30.8 (0.22)	6.8 (0.24)
<b>Goke 2010 N=858</b>	52	HbA1c: 6.5-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d	Saxagliptin 5 mg QD	Age: 57.5 (0.50) Males: 50%	7.7 (0.04)	NR	88.7 (0.90)	31.5 (0.28)	5.5 (0.22)
			Glipizide 5-20 mg QD	Age: 57.6 (0.50) Males: 54%	7.7 (0.04)	NR	88.6 (0.95)	31.3 (0.30)	5.4 (0.23)
<b>Pratley 2010 N=665</b>	26	HbA1c: 7.5-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d BMI: ≤45 kg/m <sup>2</sup>	Liraglutide 1.2 mg QD	Age: 55.9 (0.6) Males: 52%	8.4 (0.05)	131.2 (0.96)	93.7 (1.23)	32.6 (0.35)	6.0 (0.30)
			Liraglutide 1.8 mg QD	Age: 55.0 (0.6) Males: 52%	8.4 (0.05)	133.4 (0.98)	94.6 (1.22)	33.1 (0.34)	6.4 (0.36)
			Sitagliptin 100 mg QD	Age: 55.0 (0.6) Males: 55%	8.5 (0.05)	132.1 (1.00)	93.1 (1.28)	32.6 (0.36)	6.3 (0.36)

<b>Rigby 2010 N=169</b>	16	HbA1c: 7-10% Stable therapy for ≥12 weeks Metformin Dose: 1500-2550 mg/d BMI: ≤40 kg/m <sup>2</sup>	Colesvelam 3.75 g QD	Age: 56.6 (1.22) Males: 49%	8.1 (0.10)	NR	78.7 (2.45)	NR	8.1 (0.79)
			Rosiglitazone 4 mg QD	Age: 54.7 (1.46) Males: 41%	8.1 (0.10)	NR	81.1 (2.39)	NR	7.6 (0.80)
			Sitagliptin 100 mg QD	Age: 54.8 (1.31) Males: 36%	8.2 (0.12)	NR	79.6 (2.42)	NR	8.4 (0.94)
<b>Scheen 2010 N=801</b>	18	HbA1c: 6.5-10% Stable therapy for ≥8 weeks Metformin Dose: ≥1500 mg/d	Saxagliptin 5 mg QD	Age: 58.8 (0.50) Males: 47%	7.7 (0.05)	NR	NR	31.1 (0.26)	6.3 (0.25)
			Sitagliptin 100 mg QD	Age: 58.1 (0.53) Males: 51%	7.7 (0.05)	NR	NR	30.9 (0.28)	6.3 (0.24)
<b>DeFronzo 2009 N=743</b>	24	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: 1500-2550 mg/d BMI: ≤40 kg/m <sup>2</sup>	Placebo	Age: 54.8 (0.76) Males: 54%	8.1 (0.07)	NR	87.1 (1.33)	31.6 (0.36)	6.7 (0.42)
			Saxagliptin 2.5 mg QD	Age: 54.7 (0.73) Males: 43%	8.1 (0.07)	NR	86.0 (1.27)	31.7 (0.38)	6.7 (0.40)
			Saxagliptin 5 mg QD	Age: 54.7 (0.69) Males: 54%	8.1 (0.06)	NR	87.3 (1.23)	31.2 (0.34)	6.4 (0.34)
<b>Ferrannini 2009 N=2789</b>	52	HbA1c: 6.5-8.5% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d BMI: 22-45 kg/m <sup>2</sup>	Vildagliptin 50mg BID	Age: 57.5 (0.24) Males: 53%	7.3 (0.02)	NR	89.0 (NR)	31.8 (0.14)	5.7 (0.14)
			Glimeperide 2 to 6 mg QD	Age: 57.5 (0.25) Males: 54%	7.3 (0.02)	NR	88.6 (NR)	31.7 (0.14)	5.8 (0.13)
<b>Goodman 2009 N=370</b>	24	HbA1c: 7.5-11% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg BMI: 22-40 kg/m <sup>2</sup> FPG: <270 mg/dl	Vildagliptin 100 mg QD	Age: 54.9 (0.69) Males: 53%	8.5 (0.06)	NR	NR	31.4 (0.30)	NR
			Placebo	Age: 54.5 (0.88) Males: 67%	8.7 (0.10)	NR	NR	31.7 (0.39)	NR
<b>Nauck 2009 N=527</b>	26	HbA1c: 7-10% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d BMI: 23-45 kg/m <sup>2</sup> FPG: <275 mg/dl	Placebo	Age: 56 (1.08) Males: 48%	8.0 (0.09)	129 (1.67)	NR	32 (0.59)	6 (0.49)
			Alogliptin 12.5 mg QD	Age: 55 (0.75) Males: 47%	7.9 (0.05)	127 (0.89)	NR	32 (0.34)	6 (0.34)
			Alogliptin 25 mg QD	Age: 54 (0.76) Males: 54%	7.9 (0.06)	127.3 (1.03)	NR	32 (0.35)	6 (0.28)
<b>Nauck 2009 N=1087</b>	26	HbA1c: 7-11% Therapy with mono- or dual OAD ≥12 weeks 3 week metformin titration to 2 g/d then a 3 week stabilization period BMI: ≤40 kg/m <sup>2</sup>	Liraglutide 0.6 mg QD	Age: 56 (0.71) Males: 62%	8.4 (0.06)	131 (0.90)	NR	30.5 (0.31)	7 (0.32)
			Liraglutide 1.2 mg QD	Age: 57 (0.58) Males: 54%	8.3 (0.06)	132 (0.90)	NR	31.1 (0.31)	7 (0.32)
			Liraglutide 1.8 mg QD	Age: 57 (0.58) Males: 59%	8.4 (0.06)	131 (0.90)	NR	30.9 (0.30)	8 (0.32)
			Glimepiride 4 mg QD	Age: 57 (0.58) Males: 57%	8.4 (0.06)	132 (1.03)	NR	31.2 (0.30)	8 (0.32)
			Placebo	Age: 56 (0.82) Males: 60%	8.4 (0.10)	135 (1.45)	NR	31.6 (0.40)	8 (0.55)

<b>Hamann 2008 N=596</b>	52	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: ≥850 mg/d If taking ≥1.5 g/d entered a 4 week titration with 2 g/d. If taking <1.5 g/d entered an additional 1 week titration with 1.5 g/d before entering 4 week titration with 2 g/d BMI: ≥25 kg/m <sup>2</sup>	Rosiglitazone/metformin 4 mg QD	Age: 58.5 (0.56) Males: 53%	8.0 (0.05)	NR	91.4 (1.00)	33.0 (0.34)	6.3 (0.31)
			Glibenclamide 5 mg QD	Age: 59.3 (0.53) Males: 52%	8.0 (0.06)	NR	88.9 (0.96)	32.2 (0.28)	6.4 (0.32)
			Gliclazide 80 mg QD						
<b>Khanolkar 2008 N=50</b>	24	HbA1c: >6.5% If <2 g/d metformin, entered 4week titration, when max tolerated dose was reached (up to 2 g/d) then entered a 4week stabilization	Rosiglitazone 4 mg QD	Age: 59 (NR) Males: 56%	7.3 (0.10)	NR	NR	34.6 (1.77)	NR
			Gliclazide 80 mg QD	Age: 56 (NR) Males: 60%	7.1 (0.14)	NR	NR	33.7 (1.64)	NR
<b>Raz 2008 N=190</b>	30	HbA1c: 8-11% Therapy with mono- or dual OAD. OAD(s) switched to metformin 1500-2550 mg/d and entered a 6 week stabilization FPG: 129.7-281.1 mg/dl	Sitagliptin 100 mg QD	Age: 53.6 (0.97) Males: 51%	9.3 (0.09)	NR	81.5 (1.71)	30.1 (0.45)	8.4 (0.66)
			Placebo	Age: 56.1 (0.98) Males: 42%	9.1 (0.08)	NR	81.2 (2.00)	30.4 (0.55)	7.3 (0.55)
<b>Scott 2008 N=273</b>	18	HbA1c: 7-11% Stable therapy for ≥10 weeks Metformin Dose: ≥1500 mg/d FPG: <270 mg/dl	Placebo	Age: 55.3 (0.97) Males: 59%	7.7 (0.09)	NR	84.6 (1.72)	30.0 (0.47)	5.4 (0.39)
			Sitagliptin 100 mg QD	Age: 55.2 (1.01) Males: 55%	7.8 (0.10)	NR	83.1 (1.76)	30.3 (0.48)	4.9 (0.36)
			Rosiglitazone 8 mg QD	Age: 54.8 (1.13) Males: 63%	7.7 (0.09)	NR	84.9 (1.98)	30.4 (0.59)	4.6 (0.43)
<b>Bosi 2007 N=544</b>	24	HbA1c: 7.5-11% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d If tolerated, increased to 2 g/d at visit 1 BMI: 22-45 kg/m <sup>2</sup> FPG: < 270.3 mg/dl	Vildagliptin 50 mg QD	Age: 54.3 (0.73) Males: 57%	8.4 (0.07)	NR	NR	32.1 (0.40)	6.8 (0.41)
			Vildagliptin 100 mg QD	Age: 53.9 (0.70) Males: 62%	8.4 (0.07)	NR	NR	32.9 (0.37)	5.8 (0.35)
			Placebo	Age: 54.5 (0.76) Males: 53%	8.3 (0.07)	NR	NR	33.2 (0.45)	6.2 (0.39)
<b>Nauck 2007 N=1172</b>	52	HbA1c: 6.5-10% Metformin Dose: ≥1.5 g/d If not on a OAD, or on dual-OAD then entered a metformin monotherapy titration and stabilization for 8weeks	Sitagliptin 100 mg QD	Age: 56.8 (0.38) Males: 57%	7.7 (0.04)	NR	89.5 (0.72)	31.2 (0.21)	6.5 (0.25)
			Glipizide 5 – 20 mg QD	Age: 56.9 (0.41) Males: 61%	7.6 (0.04)	NR	89.7 (0.72)	31.3 (0.22)	6.2 (0.22)
<b>Ristic 2006 N=262</b>	24	HbA1c: 6.8-9% Stable therapy for ≥8 weeks Metformin Dose: ≥1000 mg/d (or maximum tolerated dose) BMI: 20-35 kg/m <sup>2</sup>	Nateglinide 60 – 180 mg TID	Age: 62.0 (0.95) Males: 54%	7.7 (0.05)	NR	NR	28.5 (0.30)	7.2 (0.55)
			Gliclazide 80 – 240 mg QD	Age: 61.6 (0.89) Males: 50%	7.6 (0.05)	NR	NR	29.5 (0.32)	6.7 (0.49)

<b>DeFronzo 2005 N=336</b>	30	HbA1c: 7.1-11% Stable therapy for ≥12 weeks Metformin Dose: ≥1500 mg/d BMI: 27-45 kg/m <sup>2</sup> FPG: <240 mg/dl Weight: Stable (<10% variance) for ≥12 weeks before screening	Placebo	Age: 54 (0.84) Males: 59%	8.2 (0.09)	NR	100 (1.79)	34 (0.56)	6.6 (0.57)
			Exenatide 5 ug BID	Age: 53 (1.05) Males: 52%	8.3 (0.10)	NR	100 (2.10)	34 (0.57)	6.2 (0.56)
			Exenatide 10 ug BID	Age: 52 (1.03) Males: 60%	8.2 (0.09)	NR	101 (1.88)	34 (0.56)	4.9 (0.44)
<b>Feinglos 2005 N=122</b>	16	HbA1c: 7-8.5% Stable therapy for ≥12 weeks Metformin Dose: ≥1 g/d BMI: 27-38 kg/m <sup>2</sup>	Glipizide 2.5 mg QD	Age: 57.7 (1.37) Males: 46%	7.5 (NR)	NR	90.0 (2.39)	31.7 (0.56)	6.5 (NR)
			Placebo	Age: 58.8 (1.28) Males: 41%	7.6 (NR)	NR	90.8 (2.36)	32.1 (0.63)	4.6 (NR)
<b>Matthews 2005 N=630</b>	52	HbA1c: 7.5-11% Stable therapy for ≥12 weeks Metformin Dose: ≥50% maximum recommended dose or maximum tolerated dose	Pioglitazone 15 – 45 mg QD	Age: 56 (0.52) Males: 51%	8.7 (0.06)	NR	91.8 (0.91)	32.6 (0.28)	5.8 (0.29)
			Glucicazide 80 – 320 mg QD	Age: 57 (0.51) Males: 49%	8.5 (0.05)	NR	92.7 (0.98)	32.6 (0.33)	5.5 (0.29)
<b>Ahren 2004 N=71</b>	12	HbA1c: 7-9.5% Stable therapy for ≥12 weeks Metformin Dose: 1.5-3 g/d BMI: 20-35 kg/m <sup>2</sup>	Vildagliptin 50 mg QD	Age: 58.4 (1.42) Males: 62%	7.6 (0.09)	NR	NR	29.6 (0.57)	5.8 (0.65)
			Placebo	Age: 54.3 (2.27) Males: 76%	7.8 (0.11)	NR	NR	29.9 (0.67)	4.6 (0.67)
<b>Gomez- Perez 2002 N=116</b>	26	FPG: 140-300 mg/dl 3-6 week titration with 2.5 g/d then 4 week stabilization period	Placebo	Age: 53.4 (1.29) Males: 29%	NR	NR	NR	28.5 (0.67)	9.1 (0.96)
			Rosiglitazone 2 mg QD	Age: 51.7 (1.45) Males: 29%	NR	NR	NR	28.0 (0.68)	11.1 (1.20)
			Rosiglitazone 4 mg QD	Age: 54.2 (1.55) Males: 19%	NR	NR	NR	27.6 (0.53)	10.7 (1.17)
<b>Marre 2002 N=467</b>	24	HbA1c: 6.8-11% Stable therapy for ≥4 weeks Metformin Dose: ≥1500 mg/d 4 week 2 g/d stabilization period BMI: 20-35 kg/m <sup>2</sup>	Nateglinide 60 mg TID	Age: 57.9 (0.80) Males: 61%	8.0 (NR)	NR	84.8 (1.1)	29.4 (0.30)	7.2 (0.51)
			Nateglinide 120 mg TID	Age: 57.3 (0.83) Males: 61%	8.2 (NR)	NR	85.2 (1.1)	29.3 (0.28)	6.8 (0.43)
			Placebo	Age: 56.4 (0.84) Males: 55%	8.3 (NR)	NR	84.9 (1.2)	29.6 (0.32)	6.5 (0.53)
<b>Charpentier 2001 N=372</b>	20	Stable therapy for ≥4 weeks Metformin Dose: 2550 mg/d FPG: 7.8-13.9 mmol/l BMI: 23-40 kg/m <sup>2</sup>	Placebo	Age: 56.7 (NR) Males: 60%	6.8 (0.14)	142 (1.27)	82.2 (NR)	29.2 (NR)	7.0 (NR)
			Glimepiride 1 – 6 mg QD	Age: 56.8 (NR) Males: 59%	6.4 (0.09)	140 (0.99)	81.2 (NR)	29.5 (NR)	5.6 (NR)
<b>Van Gaal 2001 N=152</b>	32	HbA1c: 7.5-10.5% Stable therapy for ≥12 weeks Metformin Dose: 1500-2550 mg/d BMI: 23-40 kg/m <sup>2</sup> Weight: Stable (<5% variance) for ≥12 weeks before enrollment	Migliitol 100 mg TID	Age: 57.9 (1.14) Males: 42%	8.5 (0.11)	NR	NR	30.0 (0.46)	6 (1.32) <sup>c</sup>
			Placebo	Age: 57.9 (0.98) Males: 49%	8.4 (0.12)	NR	NR	29.7 (0.45)	6 (0.22) <sup>c</sup>



<b>Halimi 2000 N=129</b>	24	HbA1c: 7-11% Stable therapy for ≥8 weeks Metformin Dose: 1500-2550 mg/d BMI: 25-35 kg/m <sup>2</sup>	Acarbose 50-100 mg TID	Age: 56 (1.20) Males: 48%	8.6 (0.14)	NR	NR	30.1 (0.43)	9.5 (0.97)
			Placebo	Age: 55 (1.20) Males: 63%	8.5 (0.13)	NR	NR	29.7 (0.39)	9.0 (0.90)
<b>Fonseca 2000 N=348</b>	26	Metformin Dose: ≥2.5 g/d If <2.5 g/d, entered a 3 week titration to 2.5 g/d then 4 week stabilization period BMI 22-38 kg/m <sup>2</sup> Weight: Stable (<10% variance) between screening and baseline FPG: 140-300 mg/dl	Placebo	Age: 58.8 (0.87) Males: 74%	8.6 (0.12)	NR	NR	30.3 (0.41)	7.3 (0.54)
			Rosiglitazone 4 mg QD	Age: 57.5 (0.97) Males: 62%	8.9 (0.12)	NR	NR	30.2 (0.39)	7.5 (0.58)
			Rosiglitazone 8 mg QD	Age: 58.3 (0.84) Males: 68%	8.9 (0.14)	NR	NR	29.8 (0.37)	8.3 (0.60)
<b>Moses 1999 N=83</b>	12	HbA1c: >7.1% Stable therapy: ≥6 months Metformin Dose: 1-3 g/d BMI: ≥21 kg/m <sup>2</sup>	Repaglinide 4 mg QD	Age: 57.2 (1.60) Males: 67%	8.3 (0.17)	NR	NR	33.2 (1.08)	5.9 (0.56)
			Placebo	Age: 57.8 (1.83) Males: 63%	8.6 (0.21)	NR	NR	31.8 (1.15)	8.0 (1.19)
<b>Rosenstock 1998 N=148</b>	24	HbA1c: 7-10% Stable therapy for ≥8 weeks Metformin Dose: 2 or 2.5 g/d Weight: Stable (< 3 kg) for ≥4 weeks before screening	Acarbose 50-100 mg TID	Age: 57.2 (NR) Males: 61%	8.5 (NR)	NR	94.4 (NR)	32.4 (NR)	7.2 (NR)
			Placebo	Age: 55.9 (NR) Males: 49%	8.2 (NR)	NR	91.5 (NR)	32.3 (NR)	7.8 (NR)