Supplementary Materials

Supplemental Table S1 Results of comparative trials of GLP-1RAs and oral glucose-lowering therapies: blood pressure and lipids

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Dipeptidyl peptidase-4 inhibitors									
Berg et al 2011[1]	CO, DB, DD, R in pts with T2D [2 × 4 weeks]	ExBID 10 mcg/SITA 100 mg QD [41] SITA 100 mg QD/ExBID 10 mcg [42]	MET (n = 82) TZD (n = 1)	ExBID: –2.5 SITA: –2.0	ExBID: +1.1 SITA: –0.9	NR	NR	NR	NR
Bergenstal et al 2010[2] (DURATION-2; NCT00637273)	DB, DD, MC, PG, R in pts with T2D [26 weeks]	ExQW 2 mg [160] SITA 100 mg QD [166]	MET	ExQW: –3.6**[a] SITA: +0.2[a]	NR	ExQW: –0.02[a] SITA: +0.08[a]	ExQW: –0.03[a] SITA: +0.05[a]	ExQW: +0.05[a] SITA: +0.05[a]	No significant difference between treatments

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
		PIO 45 mg QD [165]							
Russell-Jones et al 2012[3] (DURATION-4; NCT00676338)	DB, MC, PG, R in treatment-naive pts with T2D [26 weeks]	ExQW 2 mg [248] MET 2000 mg/day [246] PIO 45 mg QD [163] SITA 100 mg QD [163]	None	ExQW: –1.3 SITA: –1.8	No changes reported for these groups	No clinically significant changes in fasting serum lipids were observed during the treatment period.			
Nauck et al 2014[4] (AWARD-5; NCT00734474)	DB, MC, PG, R in pts with T2D [52 weeks]	DULA 0.75 mg QW [302] DULA 1.5 mg QW	MET	DULA 0.75: –0.5 DULA 1.5: –0.8 SITA: –0.5	DULA 0.75: +0.2 DULA 1.5: +0.3 SITA: –0.2	DULA 0.75: –0.03 DULA 1.5: –0.03 SITA: +0.10	DULA 0.75: +0.02 DULA 1.5: –0.06** SITA: +0.12	DULA 0.75: +0.07 DULA 1.5: +0.05 SITA: +0.05	DULA 0.75: –0.15 DULA 1.5: –0.16 SITA: –0.06

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
		[304] SITA 100 mg QD [315] PBO [177]							
Weinstock et al 2015[5] (AWARD-5; NCT00734474)	DB, MC, PG, R in pts with T2D [104 weeks]	DULA 0.75 mg QW [302] DULA 1.5 mg QW [304] SITA 100 mg QD [315] PBO [177]	MET	DULA 0.75: +1.3 DULA 1.5: –0.1 SITA: <0.1	DULA 0.75: +1.4* DULA 1.5: +0.4 SITA: –0.4	No significant differences in fasting lipids were observed			
Charbonnel et al 2013[6] (NCT01296412)	OL, MC, PG, R in	LIRA 1.2 mg/day[b]	MET	LIRA: –1.9 SITA: +0.9	LIRA: +0.4 SITA: +0.8	LIRA: +0.1 SITA: +2.1	LIRA: +3.2 SITA: +7.3	LIRA: +4.6 SITA: +3.9	NR % change:

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	pts with T2D [26 weeks]	[253] SITA 100 mg OD[c] [269]							LIRA: –9.8% SITA: –10.5%
Pratley et al 2010[6] (NCT00700817)	OL, MC, PG, R in pts with T2D [26 weeks]	LIRA 1.2 mg/day [225] LIRA 1.8 mg/day [221] SITA 100 mg QD [219]	MET	LIRA 1.2: –0.55 LIRA 1.8: –0.72 SITA: –0.94	LIRA 1.2: –0.71 LIRA 1.8: +0.07 SITA: –1.78	LIRA 1.2: –0.03 LIRA 1.8: –0.17 SITA: –0.02	LIRA 1.2: +0.08 LIRA 1.8: +0.05 SITA: +0.13	LIRA 1.2: 0.00 LIRA 1.8: 0.00 SITA: 0.00	LIRA 1.2: –0.19 LIRA 1.8: –0.43 SITA: –0.40
Pratley et al 2011[7] (NCT00700817)	OL, MC, PG, R in pts with T2D [52 weeks]	LIRA 1.2 mg/day [225] LIRA 1.8 mg/day [221] SITA 100 mg QD [219]	MET	LIRA 1.2: –0.37 LIRA 1.8: –2.55 SITA: –1.03	LIRA 1.2: –0.53 LIRA 1.8: –0.87 SITA: –1.47	LIRA 1.2: –0.01 LIRA 1.8: –0.09 SITA: +0.03	LIRA 1.2: +0.09 LIRA 1.8: +0.09 SITA: +0.17	LIRA 1.2: +0.01 LIRA 1.8: +0.02 SITA: +0.01	LIRA 1.2: –0.10 LIRA 1.8: –0.32 SITA: –0.23

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Pratley et al 2012[8] (NCT00700817)	OL extension of pts with T2D completing the 1860-LIRA-DPP-4 core study [26 weeks]	SITA 100mg to LIRA 1.2 mg [67] SITA 100 mg to LIRA 1.8 mg [68]	MET	LIRA 1.2: –2.1 LIRA 1.8: +0.4	LIRA 1.2: –0.6 LIRA 1.8: 0.0	LIRA 1.2: –0.2 LIRA 1.8: –0.2†	LIRA 1.2: –0.2† LIRA 1.8: –0.3††	LIRA 1.2: 0.0 LIRA 1.8: 0.0	LIRA 1.2: –0.2 LIRA 1.8: –0.3†
Takeshita et al 2015[9]	OL, PG, R in Japanese pts with T2D not adequately	LIRA 0.9 mg QD [54] VILD 50 mg BID [58]	None	LIRA: –2.5 VILD: –7.9	NR	LIRA: –0.29†† VILD: –0.03	LIRA: 0.0[d] VILD: –0.01[d]	LIRA: –0.09 VILD: +0.02	LIRA: –0.12 VILD: –0.15

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	controlled by SITA-based therapy [12 weeks]								
Metformin									
Umpierrez et al 2014[10] (AWARD-3; NCT01126580)	DB, DD, MC, PG, R in pts with T2D [52 weeks[e]]	DULA 0.75 mg QW [270] DULA 1.5 mg QW [269] MET ≥1500 mg/day [268]	None	At 26 weeks DULA 0.75: –2.6 DULA 1.5: –1.9 MET: –0.9 At 52 weeks DULA	At 26 weeks DULA 0.75: –1.0 DULA 1.5: +0.05 MET: –0.64 At 52 weeks DULA	NR	NR	NR	NR

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
				0.75: –2.7 DULA 1.5: –0.1 MET: –1.0	0.75: –1.4 DULA 1.5: +0.3 MET: –0.4				
Sulfonylureas									
Gallwitz et al 2012[11] (EUREXA; NCT00359762)	OL, R, MC in overweight pts with T2D poorly controlled on MET [~3 years]	ExBID 10 mcg[f] [490] GLIM 1 mg TID[g] [487]	MET	ExBID: –1.9*** GLIM: +1.1	NR	NR	NR	NR	NR
Nauck et al 2009[12] (LEAD-2; NCT00318461)	DB, DD, MC, PG, R in pts with	LIRA 0.6 mg QD [242] LIRA 1.2 mg	MET	LIRA 0.6: –0.6 LIRA 1.2:	No changes	NR	NR	NR	NR

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	T2D [26 weeks]	QD [240] LIRA 1.8 mg QD [242] GLIM 4 mg QD [242] PBO [121]		–2.8* LIRA 1.8: –2.3* GLIM 4: +0.4					
Nauck et al 2013[13] (LEAD-2; NCT00318461)	OL extension of pts with T2D completing the LEAD-2 core study [18 months]	LIRA 0.6 mg QD [184] LIRA 1.2 mg QD [178] LIRA 1.8 mg QD [174] GLIM 4 mg QD [183] PBO [61]	MET	LIRA 0.6: +0.2 LIRA 1.2: –2.5 LIRA 1.8: –2.0 GLIM 4: +0.3	LIRA 0.6: +0.4 LIRA 1.2: –0.8 LIRA 1.8: –0.5 GLIM 4: 0.0	LIRA 0.6: –0.01 LIRA 1.2: +0.09 LIRA 1.8: +0.07 GLIM 4: +0.08	LIRA 0.6: –0.23 LIRA 1.2: –0.17 LIRA 1.8: –0.13 GLIM 4: –0.12	LIRA 0.6: 0.00 LIRA 1.2: –0.03 LIRA 1.8: –0.02 GLIM 4: –0.05	LIRA 0.6: –0.18 LIRA 1.2: –0.13 LIRA 1.8: –0.11 GLIM 4: +0.06
Garber et al 2009[14] (LEAD-3 Mono;	DB, DD, MC, PG, R	LIRA 1.2 mg QD [251]	None	LIRA 1.2: –2.1	Slight but NS	NR	NR	NR	NR

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
NCT00294723)	in pts with early T2D [52 weeks]	LIRA 1.8 mg QD [247] GLIM 8 mg QD [248]		LIRA 1.8: –3.6† GLIM: –0.7	decrease in all groups				
Garber et al 2011[15] (LEAD-3 Mono; NCT00294723)	OL extension of pts with T2D completing the LEAD-3 core study [52 weeks]	LIRA 1.2 mg QD [110] LIRA 1.8 mg QD [114] GLIM 8 mg QD [97]	None	LIRA 1.2: –1.35 LIRA 1.8: –2.37 GLIM: –0.49	LIRA 1.2: –0.58 LIRA 1.8: –0.81 GLIM: –0.44	NR	NR	NR	NR
Seino et al 2010[16] (NCT00393718)	DB, DD, MC, PG, R in Japanese	LIRA 0.9 mg QD [272] GLYB 1.25–2.5 mg/day	None	No significant difference between treatment groups (values not reported)		LIRA: –0.31 GLYB: –0.2	LIRA: –0.19 GLYB: –0.12	LIRA: –0.03 GLYB: –0.01	LIRA: +0.05 GLYB: +0.1

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	pts with T2D [24 weeks]	[139]							
Kaku et al 2011[17] (NCT00393718)	OL extension of Seino study in Japanese pts with T2D [52 weeks]	LIRA 0.9 mg QD [268] GLYB 1.25–2.5 mg/day [132]	None	NR	NR	Treatment difference: –0.10	Treatment difference: –0.05	Treatment difference: +0.03	Treatment difference: –0.17
Thiazolidinediones									
DeFronzo et al 2010[18] (NCT00135330)	OL, MC, PG, R in MET-treated pts with T2D	ExBID 10 mcg[f] [45] ROSI 4 mg BID[f] [45] ExBID	MET	NR	NR	ExBID: –0.13*** ROSI: +0.44	ExBID: –0.05** ROSI: +0.33	ExBID: +0.02 ROSI: +0.06	ExBID: –0.34 ROSI: +0.07

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	[20 weeks]	10 mcg + ROSI 4 mg BID[f] [47]							
Xu et al 2015[19] (CONFIDENCE; NCT01147627)	OL, MC, PG, R in treatment-naive pts with newly diagnosed T2D [48 weeks]	ExBID 10 mcg[f] [142] PIO 30–45 mg QD [136] ILis 0.2 IU/kg BID[f][138]	None	ExBID: –4† PIO: –1	ExBID: –3† PIO: –3†††	ExBID: –0.2†* PIO: –0.1	ExBID: –0.2† PIO: –0.1	ExBID: +0.08†** PIO: +0.16†††	ExBID: –0.2† PIO: –0.2
Bergenstal et al 2010[2] (DURATION-2; NCT00637273)	DB, DD, MC, PG, R in pts with T2D [26 weeks]	ExQW 2 mg [160] SITA 100 mg QD [166] PIO 45 mg QD [165]	MET	ExQW: –3.6**[a] PIO: –1.6[a]	NR	ExQW: –0.02[a] PIO: +0.16[a]	ExQW: –0.03[a] PIO: +0.05[a]	ExQW: +0.05***[a] PIO: +0.16[a]	ExQW: –0.04***[a] PIO: –0.1[a]

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Russell-Jones et al 2012[3] (DURATION-4; NCT00676338)	DB, MC, PG, R in treatment-naive pts with T2D [26 weeks]	ExQW 2 mg [248] MET 2000 mg/day [246] PIO 45 mg QD [163] SITA 100 mg QD [163]	None	ExQW: –1.3 PIO: –1.7	ExQW: NR PIO: –2.5	No clinically significant changes in fasting serum lipids were observed during the treatment period.			
Marre et al 2009[20] (LEAD-1 SU; NCT00318422)	DB, DD, MC, PG, R in pts with T2D treated with oral GLT for ≥3 months [26 weeks]	LIRA 0.6 mg/day [233] LIRA 1.2 mg/day [228] LIRA 1.8 mg/day [234] ROSI 4 mg/day [232] PBO [114]	GLIM	No significant differences between treatments (decreases of 0.9–2.8)	No significant differences between treatments (decreases of 0.7–1.4)	NR	NR	NR	NR

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides

Notes: [a] Values estimated from a figure; [b] After 12 weeks, LIRA up-titrated to 1.8 mg/day in pts with A1C ≥7.0% (53 mmol/mol) and FG >6.05 mmol/L; [c] After 12 weeks, GLIM 1 or 2 mg/day added to regimen of pts with A1C ≥7.0% (53 mmol/mol) and FG >6.05 mmol/L; [d] Data for small dense LDL; [e] Primary end point was the change from baseline in A1C at 26 weeks. Secondary end points included the change from baseline in A1C at 52 weeks, and the change from baseline in FG and BW at 26 and 52 weeks; [f] Administered at half the named dosage for the first month of the study; [g] Dosage adjusted every 4 weeks up to the maximum tolerated dosage according to country-specific labeling information. *P < 0.05; **P < 0.01; ***P ≤ 0.001, GLP-1RA vs comparator; †P < 0.05, ††P < 0.01, ††† P ≤ 0.001 vs baseline (start of extension).

Abbreviations: AWARD, Assessment of Weekly Administration of Dulaglutide in Diabetes; BID, twice daily; CO, crossover; CONFIDENCE, Comparison of Glycaemic Control and β-Cell Function Amongst Newly Diagnosed Patients With Type 2 Diabetes Treated With Exenatide, Insulin or Pioglitazone: A Multicentre Randomized Parallel-Group Study; DBP, diastolic blood pressure; DD, double dummy; DULA, dulaglutide; DURATION, Diabetes Therapy Utilization: Researching Changes in A1c, Weight and Other Factors Through Intervention With Exenatide Once Weekly; EUREXA, European Exenatide Study; ExBID, exenatide twice daily; ExQW, exenatide once weekly; GLIM, glimepiride; GLP-1RA, glucagon-like peptide-1 receptor agonist; GLT, glucose-lowering therapy; GLYB, glyburide; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LEAD, Liraglutide Effect and Action in Diabetes; LIRA, liraglutide; LIXI, lixisenatide; MC, multicenter; MET, metformin; NR, not reported; OL, open label; PBO, placebo; PG, parallel group; PIO, pioglitazone; pts, patients; QD, once daily; QW, once weekly; R, randomized; ROSI, rosiglitazone; SB, single blind; SBP, systolic blood pressure; SITA, sitagliptin; T2D, type 2 diabetes; TID, three times a day; TZD, thiazolidinedione; VILD, vildagliptin.

Supplemental Table S2 Results of retrospective trials of GLP-1RAs and oral glucose-lowering therapies or insulins: blood pressure and lipids

Publication	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Dipeptidyl peptidase-4 inhibitors									
Horton et al 2010[21]	Retrospective analysis of adult pts with T2D using data from the GEC database [3–12 months]	EXE [6280] INS [32,398] SITA [5861]	OADs	EXE: –2.3 SITA: –1.1	EXE: –1.2 SITA: –0.6	EXE: –0.28 SITA: –0.26	EXE: –0.10 SITA: –0.16	EXE: –0.01 SITA: –0.02	EXE: –0.30 SITA: –0.23
Nyeland et al 2015[22]	Retrospective database analysis of adult pts with T2D in primary care in UK [6 months]	LIRA [287] SITA [2781]	OADs	LIRA: –3.91 SITA: –0.38***	NR	NR	NR	NR	NR
Insulins									
Horton et al 2010[21]	Retrospective analysis of pts with	EXE [6280] INS	OADs	EXE: –2.3 INS: –1.8	EXE: –1.2 INS: –1.3	EXE: –0.28 INS: –0.36	EXE: –0.10 INS: –0.21	EXE: –0.01 INS: –0.01	EXE: –0.30 INS: –0.51

Publication	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	T2D using data from the GEC database [3–12 months]	[32,398] SITA [5861]							
Pawaskar et al 2012[23] Diabetes Obes Metab	Retrospective analysis of adult pts with T2D using data from the GEC database [1 year]	EXE [4494] IG [5424]	OADs	EXE: –1.8** IG: –0.1	EXE: –0.7 IG: –0.9	EXE: –0.20 IG: –0.21	EXE: –0.11 IG: –0.07	EXE: –0.00 IG: –0.01	EXE: –0.19 IG: –0.24
Pawaskar et al 2012[24] Curr Med Res Opin	Retrospective analysis of elderly pts (≥65 years] with T2D using data from the GEC database [1 year]	EXE [1023] IG [2238]	OADs	EXE: –2.2* IG: +1.0	EXE: –0.8 IG: –0.7	NR	NR	NR	NR
Sudhakaran et al 2010[25]	Retrospective analysis of adult	ExBID 5–10 mcg [47]	OADs	EXE: –2 IG: +2	EXE: –1 IG: –1	EXE: –0.3 IG: –0.3	EXE: –0.4 IG: –0.5	EXE: –0.1 IG: 0.0	EXE: –0.1 IG: –0.1

Publication	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs comparator					
				Blood pressure (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	pts with T2D in India [24 weeks]	IG QD or BID [54] NPH QD or BID [23]		NPH: –4	NPH: –1	NPH: –0.1	NPH: –0.2	NPH: –0.1	NPH: –0.1
Sulfonylureas									
Chiefari et al 2015[26]	Retrospective analysis in adult out-pts with T2D in Italy [18 months]	LIRA 1.8 mg/day [76] GLIM 4 mg/day [103]	MET	LIRA: –10.0*** GLIM: 0.0	LIRA: 0.0** GLIM: 0.0	LIRA: –0.30 GLIM: –0.16	NR	LIRA: +0.05 GLIM: +0.03	LIRA: –0.07 GLIM: +0.05

Notes: *P < 0.05; **P < 0.01; ***P ≤ 0.001, GLP-1RA vs comparator.

Abbreviations: BID, twice daily; ExBID, exenatide twice daily; EXE, exenatide; GEC, General Electric Centricity; GLP-1RA, glucagon-like peptide-1 receptor agonist; GLIM, glimepiride; IDet, insulin detemir; IG, insulin glargine; INS, insulin; LAI, long-acting insulin; LIRA, liraglutide; OAD, oral antidiabetes drug; NPH, neutral protamine Hagedorn insulin; NR, not reported; pts, patients; QD, once daily; RAI, rapid-acting insulin; SITA, sitagliptin; T2D, type 2 diabetes; VHA, Veterans Health Administration; VILD, vildagliptin.

Supplemental Table S3 Results of prospective (randomized controlled and noninterventional) trials of GLP-1RAs versus insulins: blood pressure and lipids

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Insulin									
Östenson et al 2013[27] (CHOICE; NCT00635492)	MC, O study in pts with T2D [12 months]	ExBID [1096] INS [1239]	OADs	ExBID: –2.4 INS: –2.5	ExBID: –1.6 INS: –1.8	ExBID: –0.2 INS: –0.3	ExBID: –0.1 INS: –0.2	ExBID: 0.0 INS: +0.1	ExBID: –0.3 INS: –0.4
Mathieu et al 2013[28] (CHOICE; NCT00635492)	MC, O study in pts with T2D [24 months]	ExBID [1114] INS [1274]	OADs	ExBID: –3.1 INS: –3.5	ExBID: –3.2 INS: –2.0	ExBID: –0.3 INS: –0.4	ExBID: –0.2 INS: –0.3	ExBID: 0.0 INS: +0.1	ExBID: –0.4 INS: –0.4
Insulin aspart									
Nauck et al 2007[29] (NCT00082407)	MC, OL, PG, R in pts with T2D [52 weeks]	ExBID 5–10 mcg [253] Biphasic IAsp [248]	SU	ExBID: –5††† IAsp: +1	ExBID: –2† IAsp: +1	No significant changes from baseline		Treatment difference –0.04*	No significant change from baseline

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Mathieu et al 2014[30] (BEGIN: VICTOZA ADD-ON; NCT01388361)	MC, OL, PG, R in insulin-naive pts with T2D [26 weeks]	LIRA 0.6–1.8 mg/day [88] IAsp [89][a]	IDeg MET	NR	NR	No clinically relevant differences from baseline to end of trial or between groups in lipids.			
Insulin degludec									
Gough et al 2015[31] (DUAL-1; NCT01336023)	Extension of DUAL I in pts with T2D [52 weeks]	IDeg/LIRA QD [665] LIRA 0.6–1.8 mg QD [313] IDeg QD [333]	MET PIO	No significant differences between IDeg QD and LIRA		NR	NR	NR	NR
Insulin detemir									
Davies et al 2013[32] (NCT01003184)	MC, OL, PG, R in pts with T2D [26 weeks]	ExQW 2 mg [111] IDet QD or BID [105]	MET ± SU	ExQW: –6.8 IDet: –2.4	ExQW: –0.4 IDet: –0.3	ExQW: –0.1 IDet: +0.1	ExQW: –0.1 IDet: +0.03	ExQW: +0.02 IDet: +0.04	ExQW: –0.01 IDet: –0.1

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Insulin glargine									
Davies et al 2009[33] (HEELA)	MC, OL, PG, R in pts with T2D [26 weeks]	ExBID 5–10 mcg [118] IG [117]	MET SU TZD	ExBID: –2.9† IG: +0.7	ExBID: –0.5 IG: +0.9	ExBID: –0.36††† IG: –0.21††	ExBID: –0.25†† IG: –0.07	ExBID: +0.01 IG: +0.02	ExBID: –0.33††† IG: –0.38†††
Diamant et al 2010[34] (DURATION-3; NCT00641056)	MC, OL, PG, R in pts with T2D [26 weeks]	ExQW 2 mg [233] IG QD [223]	MET ± SU	ExQW: –3† IG: –1	ExQW: –1 IG: –1	ExQW: –0.12† IG: –0.04	ExQW: –0.05 IG: +0.04	ExQW: 0.00 IG: +0.01	NR (ratio of week 26 to baseline ExQW: 0.96 IG: 0.89)
Diamant et al 2012[35] (DURATION-3 extension; NCT00641056)	OL extension of DURATION-3 in pts with T2D [84 weeks]	ExQW 2 mg [233] IG QD [234]	MET ± SU	ExQW: –4.2[b] IG: –0.8	ExQW: –1.5[b] IG: –1.4[b]	ExQW: –0.12[b] IG: –0.19[c]	NR	NR	ExQW: +0.95 IG: +0.89[b]
Diamant et al 2014[36] (DURATION-3	OL extension of	ExQW 2 mg [194]	MET ± SU	ExQW: –2	ExQW: –2	ExQW: –0.13	ExQW: –0.17†††	ExQW: +0.05††	ExQW: +1.02

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
extension; NCT00641056)	DURATION-3 in pts with T2D [156 weeks]	IG QD [196]		IG: +2	IG: –2	IG: –0.07	IG: –0.13†	IG: +0.05††	IG: +0.97
Inagaki et al 2012[37] (NCT00935532)	MC, OL, PG, R in Japanese pts with T2D [26 weeks]	ExQW 2 mg [215] IG [212]	BG ± TZD	NR	NR	ExQW: –0.37*** IG: –0.16	ExQW: –0.33*** IG: –0.15	ExQW: –0.03 IG: –0.02	ExQW: +0.01 IG: +0.01
Araki et al 2015[38] (NCT01584232)	MC, OL, PG, R in Japanese pts with T2D [26 weeks]	DULA 0.75 mg QW [181] IG QD [180]	BG ± SU	DULA 0.75: +0.4 IG: +2.7	DULA 0.75: +0.3 IG: +0.3	NR	NR	NR	NR
Blonde et al 2015[39] (AWARD-4; NCT01191268)	MC, OL, PG, R in pts with T2D [52 weeks]	DULA 0.75 mg QW [293] DULA 1.5	ILis MET	DULA 0.75: +1.04 DULA	DULA 0.75: +0.15 DULA	DULA 0.75: +0.94% DULA	DULA 0.75: –1.02% DULA	DULA 0.75: +3.54%*** DULA	DULA 0.75: +5.73% DULA

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
		mg QW [295] IG QD [296]		1.5: –0.26 IG: +1.98	1.5: –0.01 IG: –0.34	1.5: 0% IG: +1.80%	1.5: –1.95% IG: +1.79%	1.5: +2.44%*** IG: –2.56%	1.5: 2.96% IG: +3.70%
D'Alessio et al 2015[40] (EAGLE)	MC, OL, PG, R in pts with T2D [24 weeks]	LIRA 0.6–1.8 mg QD [489] IG QD [489]	MET ± SU	LIRA: –3.1*** IG: –0.1	LIRA: –0.9 IG: –0.3	LIRA: –0.3 IG: –0.2	LIRA: –0.2* IG: –0.0	LIRA: –0.0*** IG: +0.0	LIRA: –0.3** IG: –0.5
Giorgino et al 2015[41] (AWARD-2; NCT01075282)	MC, OL, PG, R in pts with T2D [78 weeks]	DULA 0.75 mg QW [272] DULA 1.5 mg QW [273] IG QD [262]	MET GLIM	DULA 0.75: –0.59 DULA 1.5: –0.70 IG: +0.51	DULA 0.75: –0.36 DULA 1.5: –0.44 IG: –1.04	DULA 0.75: +0.03 DULA 1.5: +0.02 IG: +0.02	DULA 0.75: –0.02 DULA 1.5: 0 IG: +0.03	DULA 0.75: –0.02 DULA 1.5: 0 IG: –0.04	DULA 0.75: +0.03 DULA 1.5: +0.05 IG: 0

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Russell-Jones et al 2009[42] (LEAD-5; NCT00331851)	MC, OL, PG, R in pts with T2D [26 weeks]	LIRA 1.8 mg QD [230] IG QD [232] PBO [114]	MET GLIM	LIRA: –4.0*** IG: +0.54	No significant difference between LIRA and IG	NR	NR	NR	NR
Insulin lispro									
Diamant et al 2014[43] (NCT00960661)	MC, OL, PG, R in pts with T2D [30 weeks]	ExBID 5–10 mcg [315] ILis TID [312]	MET IG	ExBID: –4.1 ILis: +0.4	ExBID: –0.6 ILis: –0.1	ExBID: –0.1 ILis: –0.0	ExBID: –0.1 ILis: –0.0	ExBID: –0.04 ILis: +0.03	ExBID: +0.06 ILis: –0.05
Xu et al 2015[19] (CONFIDENCE; NCT01147627)	MC, OL, PG, R in treatment-naive pts with newly diagnosed	ExBID 5–10 mcg [142] PIO 30–45 mg QD [136]	None	ExBID: –4† ILis: 0	ExBID: –3† ILis: –1	ExBID: –0.2† ILis: –0.1	ExBID: –0.2† ILis: –0.2§	ExBID: +0.08† ILis: +0.16	ExBID: –0.2† ILis: +0.4

Publication (acronym/ ClinicalTrials.gov record)	Study design [study duration]	Treatment [patient number]	Background therapy	Change from baseline at study end, GLP-1RAs vs insulin					
				BP (mm Hg)		Lipid parameters (mmol/L)			
				SBP	DBP	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
	T2D [48 weeks]	ILis BID [138]							

Notes: [a] Treatment arms were also compared with a nonrandomized group of patients who received IDeg alone (n = 236); [b] Significantly different from baseline; *P* value not reported. **P* < 0.05; ***P* < 0.01; ****P* ≤ 0.001, GLP-1RA vs INS comparator; †*P* < 0.05, ††*P* < 0.01, †††*P* ≤ 0.001 vs baseline.

Abbreviations: AWARD, Assessment of Weekly Administration of Dulaglutide in Diabetes; BG, biguanide; BID, twice daily; CHOICE, Changes to Treatment and Outcomes in Patients With Type 2 Diabetes Initiating Injectable Therapy; CO, crossover; CONFIDENCE, Comparison of Glycaemic Control and β-Cell Function Amongst Newly Diagnosed Patients With Type 2 Diabetes Treated With Exenatide, Insulin or Pioglitazone: A Multicentre Randomized Parallel-Group Study; DBP, diastolic blood pressure; DD, double dummy; DUAL, Dual Action of Liraglutide and Insulin Degludec in Type 2 Diabetes; DULA, dulaglutide; DURATION, Diabetes Therapy Utilization: Researching Changes in A1c, Weight and Other Factors Through Intervention With Exenatide Once Weekly; EAGLE, Efficacy Assessment of Insulin Glargine vs Liraglutide After Oral Agent Failure; ExBID, exenatide twice daily; ExQW, exenatide once weekly; GLIM, glimepiride; GLP-1RA, glucagon-like peptide-1 receptor agonist; HEELA, Helping Evaluate Exenatide in Patients With Diabetes Compared With Long-Acting Insulin; IAsp, insulin aspart; IDeg, insulin degludec; IDet, insulin detemir; IG, insulin glargine; ILis, insulin lispro; INS, insulin; LEAD, Liraglutide Effect and Action in Diabetes; LIRA, liraglutide; MC, multicenter; MET, metformin; NR, not reported; OAD, oral antidiabetes drug; O, observational; OL, open label; PG, parallel group; PIO, pioglitazone; pts, patients; QD, once daily; QW, once weekly; R, randomized; SITA, sitagliptin; SU, sulfonylurea; T2D, type 2 diabetes; TID, three times daily; TZD, thiazolidinedione.

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