

## **Supplementary Material**

### **Twenty Years of Insulin Gla-100 – A Systematic Evaluation of its Efficacy and Safety in T2DM**

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**Table S1: Search Strategy**

Database	Search string																								
PubMed	((((((((Maturity onset diabet* OR Stable diabet* OR Slow onset diabet* OR Adult onset diabet*))) OR (("non-insulin dependent diabetes mellitus" OR NIDDM OR noninsulin dependent diabet*)) OR ("diabetes mellitus type 2" OR T2DM OR T2D OR Type II diabet* OR Type 2 diabet*)) OR "diabetes mellitus, type 2"[MeSH Terms])) AND (((((((("insulin glargine"[MeSH Terms] OR ("insulin glargine" OR (Insulin and Glargine))) OR (glargin* OR lantus OR Gla-100 OR Gla100 OR (glargine and U100))) OR "insulin, long-acting"[MeSH Terms] OR ("Long-acting insulin" OR "Long acting Insulin" OR ("Long acting" OR "Long-acting") AND Insulin)))) OR "Basal Insulin")) OR ("Insulin Analogue" OR "Insulin Analog")))) NOT ((Editorial[Publication Type] OR (Case report[Text Word] OR Letter[Publication Type])))																								
Embase	(((('insulin glargine':ab,ti OR (glargine OR lantus OR 'gla 100' OR gla100:ab,ti) OR ('glargine'/exp OR 'glargine':ab,ti) OR ('glargine' AND 'u100') OR ('glargine' AND 'u-100') OR ('long acting insulin'/exp OR 'long acting insulin':ab,ti) OR 'long-acting insulin':ab,ti OR ('long acting' AND 'insulin':ab,ti) OR ('basal insulin'/exp OR 'basal insulin':ab,ti) OR ('insulin analogue' OR 'insulin analog':ab,ti)) AND (('diabetes mellitus, type 2'/exp OR 'diabetes mellitus, type 2':ab,ti) OR ('diabetes mellitus type 2' OR 't2dm' OR 't2d' OR 'type ii diabetes' OR 'type 2 diabetes':ab,ti) OR ('non-insulin dependent diabetes mellitus' OR 'niddm' OR 'noninsulin dependent diabetes':ab,ti) OR ('maturity onset diabet*' OR 'stable diabet*' OR 'slow onset diabet*' OR 'adult onset diabet*':ab,ti))) NOT ('case report' OR 'letter' OR 'comment' OR 'editorial' OR 'historical article':it)) AND [humans]/lim AND [english]/lim																								
Cochrane	<table border="0"> <tr> <td data-bbox="434 932 495 963">ID</td> <td data-bbox="495 932 1899 963">Search</td> </tr> <tr> <td data-bbox="434 963 495 995">#1</td> <td data-bbox="495 963 1899 995">("insulin glargine") (Word variations have been searched)</td> </tr> <tr> <td data-bbox="434 995 495 1027">#2</td> <td data-bbox="495 995 1899 1027">MeSH descriptor: [Insulin Glargine] this term only</td> </tr> <tr> <td data-bbox="434 1027 495 1059">#3</td> <td data-bbox="495 1027 1899 1059">Insulin and Glargine</td> </tr> <tr> <td data-bbox="434 1059 495 1091">#4</td> <td data-bbox="495 1059 1899 1091">glargine or lantus or (glargine and U100) or Gla-100 or Gla100</td> </tr> <tr> <td data-bbox="434 1091 495 1123">#5</td> <td data-bbox="495 1091 1899 1123">MeSH descriptor: [Insulin, Long-Acting] this term only</td> </tr> <tr> <td data-bbox="434 1123 495 1155">#6</td> <td data-bbox="495 1123 1899 1155">"Long-acting insulin" or "Long acting Insulin"</td> </tr> <tr> <td data-bbox="434 1155 495 1187">#7</td> <td data-bbox="495 1155 1899 1187">("Long acting" or "Long-acting") AND Insulin</td> </tr> <tr> <td data-bbox="434 1187 495 1219">#8</td> <td data-bbox="495 1187 1899 1219">"Basal Insulin"</td> </tr> <tr> <td data-bbox="434 1219 495 1251">#9</td> <td data-bbox="495 1219 1899 1251">"Insulin Analogue" or "Insulin Analog"</td> </tr> <tr> <td data-bbox="434 1251 495 1283">#10</td> <td data-bbox="495 1251 1899 1283">(#1) or (#2) or (#3) or (#4) or (#5) or (#6) or (#7) or (#8) or (#9)</td> </tr> <tr> <td data-bbox="434 1283 495 1315">#11</td> <td data-bbox="495 1283 1899 1315">(#1) or (#2) or (#3) or (#4) or (#5) or (#6) or (#7) or (#9)</td> </tr> </table>	ID	Search	#1	("insulin glargine") (Word variations have been searched)	#2	MeSH descriptor: [Insulin Glargine] this term only	#3	Insulin and Glargine	#4	glargine or lantus or (glargine and U100) or Gla-100 or Gla100	#5	MeSH descriptor: [Insulin, Long-Acting] this term only	#6	"Long-acting insulin" or "Long acting Insulin"	#7	("Long acting" or "Long-acting") AND Insulin	#8	"Basal Insulin"	#9	"Insulin Analogue" or "Insulin Analog"	#10	(#1) or (#2) or (#3) or (#4) or (#5) or (#6) or (#7) or (#8) or (#9)	#11	(#1) or (#2) or (#3) or (#4) or (#5) or (#6) or (#7) or (#9)
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Database	Search string
	#12 MeSH descriptor: [Diabetes Mellitus, Type 2] this term only
	#13 ("diabetes mellitus type 2" or T2DM or T2D or "Type II diabetes" or "Type 2 diabetes"):ti,ab,kw
	#14 ("non-insulin dependent diabetes mellitus" or NIDDM or "non insulin dependent diabetes mellitus"):ti,ab,kw
	#15 "Maturity onset diabetes" or "Stable diabetes" or "Slow onset diabetes" or "Adult onset diabetes"
	#16 (#12) or (#13) or (#14) or (#15)
	#17 (#10) AND (#16) in Cochrane Reviews, Trials
	#18 (#11) AND (#16) in Cochrane Reviews, Trials

**Table S2. Response Rates (Initiation)**

Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
<b>Glargine vs. NPH</b>																
Fiesselmann, 2016 [14]	Gla-100 OD + OADs	52.2	-	43.3	-	-		-		-		38	-	-	-	
	Insulin NPH OD / BD + OADs	32.7		27.1		-		-		21.4		-		-		
Home PD, 2014 [15]	Gla-100 + OADs	50.34	-	-		-		-		-		-		25.5 (7.4)	31.8 (4.7)	-
	Insulin NPH + OADs	4.3		-		-		-		24.6 (7.6)		31 (5.7)				
Hsia SH, 2011 [17]	Insulin NPH + OADs	23.3	-	-		-		-		-		-		-	-	
	Gla-100 HS + OADs	28		-		-		-		-						
	Gla-100 morning + OADs	23.3		-		-		-		-						
Pan, 2007 [20]	Gla-100 + glimepiride 3mg	38.1	-	62.3	-	-		22.9	0.0174	-		-		-	-	
	Insulin NPH + glimepiride 3mg	30.3		58.7		-		14		-						
Eliaschewitz, 2006 [22]	Gla-100 + glimepiride 4mg	115 (50.4)	-	96 (42.1)	-	26.8	0.014	-		-		-		12.6 (5.9)	16.6 (2.6)	<0.02

Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	Insulin NPH + glimepiride 4mg	118 (48)		98 (39.8)		17.3		-		-		-		12.5 (6.3)	16 (3.3)	
Benedetti, 2003 [24]	Gla-100 OD + OADs	42	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Insulin NPH OD / BD + OADs	44		-		-		-		-		-		-	-	-
Riddle, 2003 [25]	Gla-100 + OADs	213 (58)	-	133 (36.2)	-	-	-	33.2	0.05	-	-	22.1	<0.03	-	-	
	Insulin NPH + OADs	223 (57.3)		134 (34.4)		-		26.7		-		15.9		-	-	-
Yki-Jarvinen, 2000 [26]	Gla-100 + OADs	-	-	83 (38.7)	-	-	-	-	-	-	-	-	-	-	-	
	Insulin NPH + OADs	-		66 (31.7)		-		-		-		-		-	-	-
<b>Glargine vs. Premixed Insulins</b>																
Petrovski, 2018 [27]	Human / Analog premixed alone switched to Gla-100 OD ± OADs	30.2	-	52.3	-	-		-		-		-		-	-	
Cao Y, 2017 [29]	Gla-100 OD + Sitagliptin 100mg	56.25	-	-	-	-		-		-		-		-	89.1 (12.38)	<0.05
	Insulin Aspart 30 BD	37.5		-	-	-		-		-		-		-	76.26 (14.78)	



Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction			
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)	
Buse, 2009 [33]	Lispro mix 75/25 + OADs	47.5	<0.001	-		-		-		-		-		-	-	-	
	Gla-100 + OADs	40.3		-		-		-		-		-		-			
Strojek, 2009 [32]	BI-Asp 30 + MET + SU (Glimepiride)	44.9	-	20	-	36.4		-		-		-		-	-	-	-
	Gla-100 + MET + SU (Glimepiride)	45.7		19.4		39.7		-		-		-		-			
Raskin, 2007 [36]	BiAsp 70/30 BD + MET	65	0.003	-		-		-		-		-		-	-	-	
	Gla-100 OD + MET	41		-		-		-		-		-					
Robbins, 2007 [35]	Lispro Mix 75/25 BD + MET BD	39.7	<0.005	-		-		-		-		-		-	-	-	
	Gla-100 OD + MET BD	56.3		-		-		-		-		-					
Schiel, 2007 [34]	Grp A: Gla-100 OD + Glimepiride OD													-	31.6 (7.6)		-
	Grp B: Gla-100 OD + Glimepiride OD + MET BD													-	32.6 (5)		





Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
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	Lispro Mid-mixture (50% lispro / 50% NPL)	59.3		-		-		-		-		-		-	-	
	Gla-100 OD	24.5		-		-		-		-		-		-	-	
Janka, 2005 [39]	Gla-100 + OADs (glimpeiride + metformin)	49.4	-	31.6	0.0002	-		45.5	0.0013	-		-		-	-	
	Human premixed insulin (30% regular, 70%NPH insulin; Insulin Actraphane HM 30/70)	39		15		-		28.6		-		-		-	-	
Raskin, 2005 [40]	BiAsp 70/30 BD + OADs	-		-		-		-		-		-		-	-	
	Gla-100 OD + OADs	-		-		-		-		-		-		-	-	
Malone, 2004 [41]	Sequence B (Lispro Mix 75/25 + MET 1500-2550 mg/day followed by Gla-100 HS +	42	<0.001	45	0.019	-		-		-		-		-	-	

Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	MET 1500-2550 mg/day)															
	Sequence A (Gla-100 HS + MET 1500-2550 mg/day followed by Lispro Mix 75/25 + MET 1500-2550 mg/day)	18		65		-		-		-		-		-		-
<b>Glargine vs. Second Generation Basal Insulin</b>																
Bailey, 2019 [42]	Gla-300 OD + OADs	25	0.029	-		-		-		-		-		-		-
	Gla-100 OD + OADs	21.5		-		-		-		-		-		-		-
Ghosal, 2016 [47]	IDeg 100 OD + OADs	69	-	-		-		-		-		-		-		-
	Gla-100 OD + OADs	415		-		-		-		-		-		-		-
Terauchi, 2016 [8]	Gla-300 OD ± OADs	25	-	33.9	-	23.3	-	-		28.8	-	-		-	-	-
	Gla-100 OD ± OADs	24.2		40.3		22.5		-		34.5		-		-	-	-



Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	Gla-100 OD + OADs minus DPP-4 inhibitors	48.6		-		-		-		-		-		-	-	
Zinman B, 2012 [53]	IDeg -100 + MET ± DPP-4 inhibitors	52	-	-		42	-	-		53	-	-		-	-	-
	Gla-100 OD + MET ± DPP-4 inhibitors	54		-		46		-		54		-		-	-	
Pan, 2007 [20]	Gla-100 + glimepiride 3mg	51.4	-	-		-		-		-		-		-	-	-
	Insulin NPH + glimepiride 3mg	54.2		-		-		-		-		-		-	-	
<b>Glargine vs. Co-formulations Insulin</b>																
Kumar, 2017 [54]	IDegAsp OD + metformin ± pioglitazone ± dipeptidyl peptidase-4 inhibitors	36.5	-	-		20.9		-		-		-		-	-	
	Gla-100 OD + metformin ± pioglitazone ±	40		-		23.5		-		-		-		-	-	



Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	Cohort 2 - Gla-S Impact (Gla-100 OD switched)	19.1		-		-		-		-		-		-	-	
Meneghini L, 2013 [60]	Det OD + MET	38	0.026	-		32	-	-		-		-		-	-	-
	Gla-100 OD + MET	53		-		38		-		-		-		-	-	
Esposito, 2008 [61]	Human NPL OD +OADs minus night-time SU, replaced with MET	62	-	40	-	-		-		-		-		-	-	
	Gla-100 OD +OADs minus night-time SU, replaced with MET	64		41		-		-		-		-		-	-	
Rosenstock, 2008 [9]	IDet OD + OADs	52	-	46	<0.01	-		-		-		-		-	-	
	Gla-100 OD + OADs	52		58		-		-		-		-		-	-	
Malone, 2005 [62]	Seq B - Lispro mix 75/25 BD + MET followed by Gla-100 OD	30	0.002	34	0.01	-		-		-		-		-	-	

Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	Seq A - Gla-100 OD + MET followed by Lispro mix 75/25 BD	12		51		-		-		-		-		-	-	

BD, bi- daily; DPP-4, dipeptidyl peptidase-4; IDeg, insulin degludec; Gla-100, glargine-100; Gla-300, glargine-300; MET, metformin; NPH, neutral protamine hagedorn; OADs, oral anti-diabetics, OD, once daily; RCT, randomized clinical trial; SU, sulfonylurea; TID, thrice a day.

**Table S3. Response Rates (Intensification)**

Author (year)	Intervention	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Intergroup p-value	Proportion of patients achieving target FPG [ n (if available) (%)]	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycaemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
<b>Glargine vs. NPH</b>																
Rosenstock, 2001 [73]	Gla-100 OD ± premeal regular insulin	-	-	23.6	-	-	-	-	-	-	-	-	-	-	-	-
	NPH insulin OD / BD ± premeal regular insulin	-	-	27.1	-	-	-	-	-	-	-	-	-	-	-	-
<b>Glargine vs. Premixed Insulins</b>																
Aschner, 2015 [74]	Gla-100 OD + glulisine OD before main meal + MET ± SU	43.2	<0.005	-	-	33.2	-	-	-	-	-	-	-	-	-	-
	Premixed insulin BD MET ± SU	52.6	-	-	-	31.4	-	-	-	-	-	-	-	-	-	-
Ito H, 2014 [71]	Human premixed insulin 50/50 switched to	-	-	-	-	-	-	-	-	-	-	-	-	23.7 (7.1)	24.5 (6.4)	-

















Author (year)	Intervention	Proportion of patients achieving target HbA1c [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving target FPG [n (if available)] (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no confirmed hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving HbA1c with no nocturnal hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving FPG target with no confirmed nocturnal hypoglycaemia (%)	Intergroup p-value	Proportion of patients achieving FPG with no nocturnal hypoglycaemia (%)	Intergroup p-value	Treatment Satisfaction		
														Baseline score (SD)	Post-treatment score (SD)	p-value (intergroup)
	Premixed BD switched to Gla-100 OD + rapid acting insulin	29.6		-		-		-		-		-		-	-	

BD, bi- daily; DPP-4, dipeptidyl peptidase-4; IDeg, insulin degludec; Gla-100, glargine-100; Gla-300, glargine-300; MET, metformin; NPH, neutral protamine hagedorn; OADs, oral anti-diabetics, OD, once daily; RCT, randomized clinical trial; SU, sulfonylurea; TID, thrice a day.

**Table S4.** Glycemic Variability (Initiation)

Author (year)	Glycaemic variability
<b>Gla-100 vs. NPH</b>	
Riddle, 2003 [25]	a. Mean deviation from the median of fasting values for individual subjects was greater with NPH than glargine (20.36 mg/dl vs. 18.38 mg/dl; between-treatment P = 0.013, after adjustment for baseline).
Yki-Jarvinen, 2006 [21]	a. The CVs of diurnal plasma glucose (means of all diurnal profiles) were 24.0± 0.8 and 22.2±0.9% (p=0.16, NS) during the run-in period, and 29.7±0.5 and 30.4±0.5% (p=0.30, NS) during the study proper for the G+MET and NPH+ MET groups, respectively.
	b. The CVs of FPG levels during the run-in period and the study were also similar.
Pan, 2007 [20]	a. The decrease in mean daily BG was significantly greater in the insulin glargine versus the NPH-treated group (mean change 94 mg/dL vs. 80 mg/dL, p = 0.018).



Author (year)	Glycaemic variability
Mattia, 2009 [19]	a. The mean amplitude of glucose excursions (MAGE) index measured in the SMBG tended to improve between baseline and endpoint with both insulin glargine (-17.0 mg/dl; 95% CI: -34.5, 0.6 mg/dl; p = 0.058) and with NPH insulin (-13.1 mg/dl; 95% CI: -31.4, 5.3 mg/dl; p = 0.152), but there was no difference between the two insulins (p = 0.603).
	b. Mean daily BG (MDBG) measured in the SMBG improved significantly between baseline and endpoint with both insulin glargine (-40.9 mg/dL; 95% CI: -57.0, -24.8 mg/dl; p < 0.0001) and with NPH insulin (-43.9 mg/dl; 95% CI: -59.9, -27.8 mg/dl; p < 0.0001): there were no differences between the two insulins (p = 0.701).
	c. The CGMS-determined post-meal test BG profile revealed a lower BG excursion with insulin glargine than with NPH insulin (129.1 vs. 152.8; p<0.05 at 5-h post-meal test and 108.5 vs. 154.6; p < 0.01 at 6-h post-meal test
	d. Meal test blood glucose values showed better post-prandial glucose control with Gla-100 vs. NPH - 146.5 (16.7) vs. 171.2 (24.7); p < 0.02
Home PD, 2014 [15]	Mean change from baseline in daily average plasma glucose was greater with glargine than with NPH insulin (-2.5 vs. -2.2 mmol/l), with a small estimated treatment difference of -0.3 (-0.5, -0.1) mmol/l (p=0.006).
Mu P, 2011 [18]	CV of FBG was significantly lower with Gla-100 [13.4 (3.6) at baseline to 10.2 (4.2)] vs. NPH [12.9 (4) at baseline to 19.6 (6.1)]; p < 0.05
Benedetti, 2003 [24]	Mean 24-hr blood glucose value reduced similarly from baseline to end of 52 weeks of treatment for Gla-100 [37.8 (1.8)] vs. NPH [34.2 (1.8)]; p = NS
<b>Gla-100 vs. Premixed Insulins</b>	
Roach, 2006 [13]	a. Mean 24-h PG and mean 24-h PG AUC were significantly smaller for insulin lispro 25/75 plus oral agents (<0.010; 0.015).
	b. The M-value was lower for insulin lispro 25/75 plus oral agents during the in-patient test meal period (9.3 ± 6.6 vs. 14.4 ± 10.8, (P=0.020).
Robbins, 2007 [35]	a. Mean daily BG was also significantly lower with LMS0/50 + Met (8.2 [1.3] vs. 8.7 [1.9] mmol/L [147 (23) vs. 156 (35) mg/dL]; (P=0.002).
	b. The M-values were comparable between the LM50/50 + Met and G + Met groups at baseline (mean [SD], 30.6 [20.8] vs. 31.9 [24.6]; P = NS), but the M-value was significantly lower with LM50/50 + Met at end point (17.3 [13.8] vs. 25.1 [24.8]; P < 0.001).
Janka, 2005 [39]	Mean daily blood glucose level improved from 182 to 137 mg/dl in the glargine plus OAD group compared with 184 to 151 mg/dl in the 70/30 group (P < 0.0001 for between-treatment difference).
Sakharova O V 2013 [30]	The mean SMBG values were similar between groups (glargine, 150±29 vs. lispro mix, 145±31 mg/dL, p=0.572).
Cao Y, 2017 [29]	Significantly lower MPG, SD and MAGE was observed with Gla-100 + Sita vs. NOV (p<0.01)

<b>Author (year)</b>	<b>Glycaemic variability</b>
Raskin, 2005 [40]	Overall postprandial glycemic exposure was ~25% less for the BIAsp 70/30 group than for the glargine group, as demonstrated by a lower cumulative SMPG value (sum of the three mealtime plasma glucose increments) for the BIAsp 70/30 group (97.4 [90.4] vs. 129.6 [102]) mg/dL, P < 0.05).
<b>Gla-100 vs. Second Generation Basal Insulins</b>	
Pan, 2016 [46]	The within subject variability in pre-breakfast SMPG as measured by CV% was 14.2 % with IDeg and 12.9 % with IGLar (estimated treatment ratio [95 % CI] IDeg/IGlar of 1.10 [1.02 to 1.18])
Onishi Y 2013 [51]	a. The estimated within-subject day-to-day variation (CV%) in prebreakfast SMPG levels (measured during week 26 of treatment) was significantly lower for IDeg than IGLar (16.3 vs. 18.2%; treatment ratio [IDeg/IGlar]: 0.89 [95% CI 0.80 to 0.99], P = 0.013).
	b. Estimated overall mean of the nine-point SMPG profile (defined as the area under the profile divided by measurement time) was 8.1 and 7.8 mmol/L for IDeg and IGLar, respectively (ETD [IDeg – IGLar]: 0.24 mmol/L [95% CI -0.11 to 0.59], P = 0.18).
Bolli, 2015 [48]	Pre-injection mean variability measured by CV% was 18.3 (0.5) with Gla-100 and 18.7 (0.5) with a LS mean difference of 0.4 (95% CI: -1 to 1.8)
<b>Gla-100 vs. Co-formulations Insulin</b>	
Kumar, 2017 [54]	a. Mean prandial glucose increments, overall and at main evening meal, were significantly lower with IDegAsp once daily than with IGLar once daily: ETD (IDegAsp once daily IGLar once daily) P < 0.001.
	b. No statistically significant differences were identified in the mean prandial increments after breakfast and lunch.
<b>Gla-100 vs. Other Basal Insulins</b>	
Malone, 2005 [62]	a. The M-value was significantly lower with the insulin lispro mixture plus metformin (23.18 ± 20.92 vs. 31.44 ± 23.93; P = 0.001) at endpoint.
	b. MODD was not different between treatments (2.01 ± 1.25 vs. 1.96 ± 1.02 mmol/ l; P = 0.484).

**Table S5.** Glycemic Variability (Intensification)

Author (year)	Glycaemic variability			
<b>Gla-100 vs. NPH</b>				
Betonico, 2019 [72]	a.	The within-day GV was similar for both therapies; in other words, during the Gla-100 treatment mean was 49 mg/dL (range, 31-94 mg/dL), and for NPH. the mean was 51 mg/dL (range, 15-78 mg/dL).		
	b.	The average daily time spent in hyperglycaemia was lower with the Gla-100 treatment than with the INPH therapy (30% and 38%, respectively; p<0.05).		
	c.	No statistical difference was found on risk of asymptomatic hypoglycaemia between Gla-100 and NPH (p=0.54)		
<b>Gla-100 vs. Premixed Insulins</b>				
Aschner, 2015 [74]	a.	Mean daily BG declined from 185.4 (41.4) mg/dL at baseline to 142.2 (28.8) mg/dL at the end of the study with Gla-100 ( $\pm$ glulisine) and from 189 (43.2) to 138.6 (25.2) mg/dL with premixed.		
	b.	The LS mean difference between the groups was 3.6 mg/dL (95% CI 0.03–0.4); p=0.024), in favour of premixed.		
<b>Gla-100 vs. Second Generation basal Insulins</b>				
Riddle, 2014 [66]	Pre-injection, variability (coefficient of variation)			
		Gla-300	Gla-100	
	a.	Baseline (SD)	25.55 (12.41)	24.97 (11.82)
	b.	Last visit (SD)	22.21 (11.75)	21.60 (11.52)
	c.	Mean change (SD)	-3.33 (14.56)	-3.37 (14.57)
d.	LS mean change (SE)	-1.10 (1.22)	-1.08 (1.22)	



<b>Author, Year</b>	<b>Random sequence generation</b>	<b>Allocation concealment</b>	<b>Selective reporting</b>	<b>Other sources of bias</b>	<b>Blinding (participants and personnel)</b>	<b>Blinding (outcome assessment)</b>	<b>Incomplete outcome data</b>	<b>Study Quality</b>
Hsia SH, 2011 [17]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Mu P, 2011 [18]	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	Poor
Kalra, 2010 [31]	Unclear	Low	Low	Low	Low	Low	Unclear	Poor
Jain, 2010 [64]	Unclear	Unclear	Low	Low	Low	Low	Low	Poor
Strojek, 2009 [32]	Low	Low	Low	Low	Low	Low	Unclear	Fair
Mattia, 2009 [19]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Raskin, 2009 [84]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Buse, 2009 [33]	Low	Low	Low	Low	Low	Low	Low	Good
Rosenstock, 2008 [76]	Low	Low	Low	Low	Low	Low	Low	Good
Esposito, 2008 [61]	Low	Low	Low	Low	Low	Low	Low	Good
Rosenstock, 2008 [9]	Low	Low	Low	Low	Low	Low	Low	Good
Raskin, 2007 [36]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Schiel, 2007 [34]	Low	Low	Low	Low	Low	Low	Low	Good
Pan, 2007 [20]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Poor
Robbins, 2007 [35]	Low	Low	Low	Low	Low	Low	Low	Good
Eliaschewitz, 2006 [22]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Jacober, 2006 [37]	Unclear	Unclear	Low	Low	Low	Low	Low	Poor
Kazda, 2006 [10]	Unclear	Unclear	Low	Low	Low	Low	Unclear	Poor
Roach, 2006 [13]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Jarvinen, 2006 [21]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Raskin, 2005 [40]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Janka, 2005 [39]	Low	Low	Low	Low	Low	Low	Low	Good
Malone, 2005 [62]	Unclear	Unclear	Low	Low	Low	Low	Low	Poor
Shi, 2004 [23]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Poor
Malone, 2004 [41]	Low	Low	Low	Low	Low	Low	Low	Good
Benedetti, 2003 [24]	Low	Low	Unclear	Low	Low	Low	Unclear	Poor

<b>Author, Year</b>	<b>Random sequence generation</b>	<b>Allocation concealment</b>	<b>Selective reporting</b>	<b>Other sources of bias</b>	<b>Blinding (participants and personnel)</b>	<b>Blinding (outcome assessment)</b>	<b>Incomplete outcome data</b>	<b>Study Quality</b>
Riddle, 2003 [25]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Rosenstock, 2001 [73]	Unclear	Low	Low	Low	Low	Low	Low	Fair
Yki-Jarvinen, 2000 [26]	Unclear	Unclear	Low	Low	Low	Low	Unclear	Poor
Fritsche A, 2010 [64]	Unclear	Unclear	Low	Low	High	High	Low	Poor
Levin PA, 2011 [77]	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	Poor
Guigliano D, 2014 [68]	Low	Low	Low	Low	High	High	Low	Poor
Vora J, 2015 [65]	Low	Low	Low	Low	High	High	Low	Poor
Jia W, 2015 [79]	Low	Low	Low	Low	High	High	Low	Poor
Bowering K, 2012 [78]	Unclear	Unclear	Low	Unclear	High	High	Low	Poor
Miser WF, 2010 [63]	Low	Low	Unclear	Unclear	High	High	Unclear	Poor
Riddle MC, 2014 [81]	Low	Low	Low	Low	High	High	Low	Poor
Hollander P, 2008 [85]	Unclear	Unclear	Low	Low	High	High	Low	Poor

Assessment done using Cochrane Risk of Bias Tool (CRBT).

\*Thresholds for converting the CRBT scales to AHRQ standards (good, fair, and poor) as per: Penson DF, Krishnaswami S, Jules A, et al. Evaluation and Treatment of Cryptorchidism [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Dec. (Comparative Effectiveness Reviews, No. 88.) Appendix E, Quality of the Literature. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK115843/>

**Table S7:** Study quality and risk of bias indicators for observational studies

Author, Year	Study Design	Representative-ness of exposed cohorts	Selection of non-exposed cohorts	Ascertainment of exposure	Study controls for other insulin users	Assessment of outcome	Long enough follow-up	<10% lost to follow up	Stars	Study Quality*
Bailey, 2019 (DELIVER 3) [42]	Retrospective cohort	*	*	*	*	*	*		6	Good
Nakanishi, 2018 [6]	Retrospective cohort		*	*		*	*		4	Fair
Gupta, 2018 [43]	Retrospective cohort		*	*		*	*		4	Fair
Petrovski, 2018 [27]	Prospective cohort			*	*	*	*	*	5	Fair
Zhang, 2017 [28]	Prospective cohort	*		*	*	*	*	*	6	Fair
Ghosal, 2016 [47]	Retrospective cohort	*		*	*	*	*	*	6	Fair
Fiesselmann, 2016 [14]	Observational	*		*	*	*	*	*	6	Fair
Sehgal S, 2015 [7]	Retrospective cohort	*	*	*	*	*	*	*	7	Good
Ito H, 2014 [66]	Prospective cohort		*	*	*	*	*		5	Fair
Odawara M, 2014 [58]	Observational	*	*	*	*	*	*	*	7	Good
Wei W, 2014 [59]	Retrospective cohort	*	*	*	*	*	*	*	7	Good
Zhang Y, 2014 [12]	Observational		*	*	*	*	*		5	Fair
Joshi, 2005 [65]	Prospective cohort	*	*	*	*	*	*		6	Good
Tentolouris N, 2013 [83]	Retrospective cohort	*	*	*	*	*	*		6	Good
Delgado E, 2012 [16]	Comparative				*	*	*	*	4	Fair
Bullano, 2006 [38]	Retrospective cohort	*	*	*		*	*		5	Fair

Assessment done using Newcastle-Ottawa Scale.

\*Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor) as per: Penson DF, Krishnaswami S, Jules A, et al. Evaluation and Treatment of Cryptorchidism [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Dec. (Comparative Effectiveness Reviews, No. 88.) Appendix E, Quality of the Literature. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK115843/>

**Table S8:** Primary Outcomes of good quality studies

Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter- group p- value	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Inter- group p- value	Overall Hypoglycemia*	Inter- group p- value
		Baseline	Post- treatment						
<b>Gla-100 vs NPH insulin</b>									
Home PD, 2014 [15]	Gla-100 + OADs	8.2 (0.8)	7.1 (0.9)	-1.07 (0.5)	-	50.34	-	64.7 vs. 61.1	-
	Insulin NPH + OADs	8.2 (0.9)	7.2 (1.0)	-0.97 (0.5)		4.3			
<b>Gla-100 vs Premixed insulin</b>									
Sehgal S, 2015 [7]	Human NPH + OADs	10.3	8.8	-1.5	-	-	-	4.8	0.038
	Gla-100 OD + OADs	10.9	8.5	-2.4		-		16.67	
	Biphasic human premixed insulin + OADs	10.7	8.6	-2.1		-		7.1	
Cao Y, 2017 [29]	Gla-100 OD + Sitagliptin 100mg	8.07 (0.91)	-	-1.14	-	56.25	-	2.85 vs. 13.3	<0.01
	Insulin Aspart 30 BD	8.23 (0.81)	-	-0.94		37.5			
Buse, 2009 [33]	Lispro mix 75/25 + OADs	9.1 (1.3)	7.3 (1.1)	-1.8 (1.3)	0.005	47.5	<0.001	28 vs. 23.1 episodes /patient/year	0.007
	Gla-100 + OADs	9 (1.2)	7.2 (1.1)	-1.7 (1.3)		40.3			
Schiel, 2007 [34]	Grp A: Gla-100 OD + Glimepiride OD	8.22 (0.69)	7.87 (0.66)	-0.35 (0.52)	-	-	-	59 vs 72 vs. 77	-
	Grp B: Gla-100 OD + Glimepiride OD + MET BD	8.14 (0.9)	7.44 (0.92)	-0.69 (0.86)		-			
	Grp C: Human Premixed Insulin 75/25 or 70/39	8.08 (0.84)	7.83 (1.13)	-0.25 (1.02)		-			
Robbins, 2007 [35]	Lispro Mix 75/25 BD + MET BD	7.8 (0.9)	7.1 (0.9)	-0.7 (0.9)	<0.001	56.3	<0.005	0.5 vs. 0.8 episodes /patient/month	-
	Gla-100 OD + MET BD	7.8 (1)	7.5 (1.0)	-0.4 (0.9)		39.7			



Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter-group p-value	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Inter-group p-value	Overall Hypoglycemia*	Inter-group p-value
		Baseline	Post-treatment						
Janka, 2005 [39]	Gla-100 + OADs (33limepiride + metformin)	8.85 (0.98)	7.15 (0.90)	-1.64	0.0003	49.4	-	4.07 vs. 9.87 events per patient-years	<0.0001
	Human premixed insulin (30% regular, 70%NPH insulin; Insulin Actraphane HM 30/	8.83 (0.87)	7.49 (1.09)	-1.31		39			
Malone, 2004 [41]	Lispro Mix 75/25 + MET 1500-2550 mg/day followed by Gla-100 HS + MET 1500-2550 mg/day	8.7 (1.3)	7.4 (1.1)	-1.32 (1.01)	0.003	42	<0.001	0.39 vs. 0.68 episodes / patient /month	0.04
	Gla-100 HS + MET 1500-2550 mg/day followed	8.7 (1.3)	7.8 (1.1)	-0.93 (0.89)		18			
Joshi, 2005 [65]	Premixed insulin analog (Novomix 30) BD	8.79 (1.13)	7.2 (0.83)	-1.59	<0.05	45.61	<0.05	58.08 vs. 16.07	<0.05
	Gla-100 OD + Insulin Aspart TID	8.53 (1.22)	7.37 (0.83)	-1.16		32.26			
Aschner, 2015 [74]	Gla-100 OD + glulisine OD before main meal + MET ± SU	8.7 (0.9)	7.2 (0.9)	-1.48 (0.04)	0.0008	43.2	<0.005	1.20 vs. 3.40 episodes/ PYE	-
	Premixed insulin BD MET ± SU	8.7 (0.9)	7 (0.9)	-1.64 (0.04)		52.6			
Tinahones, 2014 [75]	Insulin Lispro Mix BD + MET ± Pioglitazone	8.7 (0.8)	Not mentioned	-1.3	0.010	34.5		16.51 vs. 13.07 episodes / PYE	

Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter- group p- value	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Inter- group p- value	Overall Hypoglycemia*	Inter- group p- value
		Baseline	Post- treatment						
	Gla-100 OD + Insulin Lispro OD + MET ± Pioglitazone	8.6 (0.7)	Not mentioned	-1.08		30	-		-
Tentoluris N, 2013 [83]	Premixed BD continued	8.18 (1.33)	7.58 (1.06)	-0.6	<0.001	23.2	-	0.705 vs. 0.757 episodes / patient/year	-
	Premixed BD switched to Gla- 100 OD + rapid- acting insulin	8.53 (1.29)	7.39 (0.81)	-1.14		29.6			
<b>Gla-100 vs. Second Generation Basal insulin</b>									
Bailey, 2019 [42]	Gla-300 OD + OADs	9.59 (1.96)	8.07	-1.52 (2.08)	0.003	25	0.029	9.66 vs. 12.45	-
	Gla-100 OD + OADs	9.56 (1.94)	8.26	-1.3 (2.12)		21.5			
Pan 2016 [46]	IDeg 100 OD + MET	8.3 (0.9)	7.0 (0.9)	-1.3 (1.1)	-	-	-	85 vs. 97 episodes/100PYE	-
	Gla-100 OD + MET	8.3 (0.8)	7.0 (0.9)	-1.2 (1)		-			
Bolli, 2015 [48]	Gla-300 OD + OADs (previous) - SUs / Glinides	8.49 (1.04)	7.08 (0.96)	-1.42 (0.05)	-	43.1	-	6.4 vs. 8.5 events/PYE	0.042
	Gla-100 OD + OADs (previous) - SUs / Glinides	8.58 (1.07)	7.05 (0.95)	-1.46 (0.05)		42.1			
Yki-Jarvinen, 2014 [49]	Gla-300 OD ± OADs	8.26 (0.86)	7.57	-	-	30.4	-	14.37 vs. 18.96 episodes / PYE	-
	Gla-100 OD ± OADs	8.22 (0.77)	7.56	-		30.6			
Gough SC, 2013 [50]	IDeg -200 + MET ± DPP-4 inhibitors	8.3 (1)	-	-1.3 (1.01)		52		1.22 vs. 1.42 episodes/PYE	

Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter-group p-value	Proportion of patients achieving target HbA1c [ n (if available) (%) ]	Inter-group p-value	Overall Hypoglycemia*	Inter-group p-value
		Baseline	Post-treatment						
	Gla-100 OD + MET ± DPP-4 inhibitors	8.2 (0.9)	-	-1.3 (1.01)	-	56	-		-
Onishi Y, 2013 [51]	IDeg OD + OADs minus DPP-4 inhibitors	8.4 (0.8)	7.2	-1.24	-	40.8	-	3.0 vs. 3.7 episodes/PYE	-
	Gla-100 OD + OADs minus DPP-4 inhibitors	8.5 (0.8)	7.1	-1.35		48.6			
Meneghini L, 2013 [52]	IDeg OD Flex	8.5 (1)	-	-1.28	-	38.9	-	3.6 vs. 3.6 vs. 3.5 episodes/ PYE	-
	IDeg OD in morning	8.4 (0.9)	-	-1.07		40.9			
	Gla-100 OD	8.4 (0.9)	-	-1.26		43.9			
Riddle, 2014 [66]	Gla-300 OD + meal-time insulin ± MET	8.15 (0.78)	7.25 (0.85)	-0.83 (0.06)	-	39.6	-	26.37 vs. 28.08 episodes / PYE	-
	Gla-100 OD + meal-time insulin ± MET	8.16 (0.77)	7.28 (0.92)	-0.83 (0.06)		40.9			
<b>Gla-100 vs. Co-formulation insulin</b>									
Kumar, 2016 [55]	Gla-100 OD + MET	8.9 (1)	7.6	-1.34	-	29.7	-	Treatment ratio is 1.86 in favor of Gla-100	<0.0001
	IDegAsp OD + MET	8.9 (0.9)	7.5	-1.39		33.1			
Onishi Y, 2013 [56]	IDegAsp + OADs (previous) minus DPP-4 Inhibitors / SU / Glinides	8.3 (0.8)	7 (0.8)	-1.4 (0.9)	-	-	-	1.91 vs. 2.71 episodes/ PYE	-
	Gla-100 OD + OADs (previous) minus DPP-4	8.5 (0.8)	7.3 (0.9)	-1.2 (1)		-			

Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter- group p- value	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Inter- group p- value	Overall Hypoglycemia*	Inter- group p- value
		Baseline	Post- treatment						
	Inhibitors / SU / Glinides								
<b>Gla-100 vs. Other Basal insulin</b>									
Rosenstock, 2008 [9]	IDet OD + OADs	8.64 (0.78)	7.16 (0.08)	-	-	52	-	5.8 vs. 6.2 episodes/patient- year	-
	Gla-100 OD + OADs	8.62 (0.77)	7.12 (0.08)	-		52			
Odawara M, 2014 [58]	Gla-100 OD + OADs (insulin- naive)	9.53 (1.19)	8.07 (1.2!)	-	-	-	-	-	-
	Gla-100 OD + OADs (insulin non- naive)	9.08 (1.11)	8.46 (1.39)	-		-		-	
Wei W, 2014 [59]	Cohort 1 - Gla-C Impact Gla-100 OD continued	8.6 (1.7)	8.35	-0.13	<0.05 for Gla- 100 and Det comparison in favor of Gla- 100	19.4	-	0.30 vs. 0.37 vs. 0.37 vs. 0.41 vs. 0.26 vs. 0.21 episodes /PYE	-
	Cohort 1 - Det-S Impact (Det OD switched)	8.7 (1.7)	8.64	-0.06		19.8			
	Cohort 1 - Gla-C Huma- (Gla-100 OD continued)	8.2 (1.5)	8.04	-0.14		25.8			
	Cohort 1 - Det-S Huma- (Det OD switched)	8.3 (1.5)	8.31	0		17.8			
	Cohort 2 - Det-C Impact (Det OD continued)	8.9 (1.8)	8.54	-0.68		16.9			
	Cohort 2 - Gla-S Impact (Gla-100 OD switched)	9.1 (1.9)	8.34	-0.36		19.1			
	IDet OD + MET	7.96 (0.62)	7.48 (0.91)	-0.48 (0.94)		38	0.026		

Author (Year)	Intervention	Mean change in HbA1c (SD if available)		Mean change (SD if available)	Inter- group p- value	Proportion of patients achieving target HbA1c [ n (if available) (%)]	Inter- group p- value	Overall Hypoglycemia*	Inter- group p- value
		Baseline	Post- treatment						
Meneghini L, 2013 [60]	Gla-100 OD + MET	7.86 (0.58)	7.13 (0.72)	-0.74 (0.76)	-	53	-	3.19 vs. 4.41 episodes / PYE	0.034
Esposito, 2008 [61]	Human NPL OD +OADs minus night-time SU, replaced with MET	8.8 (0.7)	-	-1.83	-	62	-	7.5 vs. 6.0 episodes/PYE	-
	Gla-100 OD +OADs minus night-time SU, replaced with MET	8.7 (0.7)	-	-1.89		64			
Rosenstock, 2008 [76]	Prandial premixed (insulin lispro protamine suspension/lispro)	8.83 (1.04)	6.95	-2.09	0.021	54	<0.05	48.70 vs. 51.20	-
	Gla-100 OD + Insulin Lispro TID +OADs (minus SU + Glinides)	8.89 (1.09)	6.78	-1.87		69			