

# Clinical trials of lispro

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 diabetes type 2

Trial	Treatments	Patients	Trials design and methods
<b>lispro thrice daily vs basal insulin</b>			
Raz , 2009 n=NA follow-up:	three premeal doses of insulin lispro versus NPH twice daily or insulin glargine once daily	patients with type 2 diabetes after acute myocardial infarction	
<b>premixed insulin lispro vs basal-bolus</b>			
Masuda , 2008 n=NA follow-up:	twice-daily 50/50 premixed insulin lispro versus NPH insulin at bedtime and preprandial insulin lispro	insulin-naive type 2 diabetic patients	
<b>lispro +glargine vs continuous infusion</b>			
Herman , 2005 n=NA follow-up:	multiple daily injection using insulin lispro and insulin glargine versus continuous subcutaneous insulin infusion using insulin lispro	-	
<b>lispro PS vs glargine</b>			
Strojek , 2010 n=NA follow-up:	insulin lispro protamine suspension (ILPS) once or twice daily versus insulin glargine once daily	-	open-label
<b>lispro mixture vs glargine once daily</b>			
Chan META-ANALYSIS , 2009 n=NA follow-up:	insulin lispro mixtures, given twice or thrice daily versus insulin glargine, given once daily	patients with type 2 diabetes treated with metformin	
<b>premix lispro 50/50 thrice time vs glargine once daily</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Robbins , 2007</b> [NCT00191464] n=158/159 follow-up: 24 weeks	lispro mix 50/50 (50% insulin lispro protamine suspension [ILPS] and 50% lispro) TID for 24 weeks versus insulin glargine QD at bedtime	patients with type 2 diabetes mellitus and an HbA(1c) level of 6.5% to 11.0% , who were receiving metformin and/or a sulfonylurea with a stable dose of 0 to 2 daily insulin injections	Parallel groups open-label Australia, Greece, India, The Netherlands, Poland, Puerto Rico, and the United States
<b>Kazda , 2006</b> n=54/53 follow-up: 24 week	3x daily lispro mid mixture (MidMix; 50% lispro, 50% protaminated lispro), versus 1x daily insulin glargine	patients with type 2 diabetes starting insulin treatment	Parallel groups open-label Germany
<b>premix lispro 75/25 twice daily vs glargine once daily</b>			
<b>DURABLE (Buse) DOUBLONS , 2011</b> n=NA follow-up:	lispro mix 75/25 twice daily versus once-daily insulin glargine	type 2 diabetes patients	
<b>DURABLE (Buse) , 2009</b> [NCT00279201] n=1045/1046 follow-up: 24 weeks	twice-daily lispro mix 75/25 versus daily glargine	patients with type 2 diabetes mellitus failing to achieve control with starter insulin treatment and continuing oral antihyperglycemic drugs	Parallel groups
<b>Malone , 2004</b> n=105/105 follow-up: 16 week	mixture of 75% insulin lispro protamine suspension and 25% insulin lispro (Mix 75/25) BID versus insulin glargine QD	patients with type 2 diabetes beginning insulin therapy	Cross over open-label USA
<b>Malone , 2005</b> n=97/97 follow-up: 32 weeks	insulin lispro mixture (25% insulin lispro and 75% NPL) twice daily versus once-daily insulin glargine	patients with Type 2 diabetes inadequately controlled with intermediate insulin, or insulin plus oral agent(s) combination therapy	Cross over
<b>premix lispro thrice daily vs glargine once daily</b>			
<b>Jacober , 2006</b> n=60/60 follow-up: 4 months	intensive insulin lispro mixture therapy for 4 months versus once-daily insulin glargine	insulin-naive patients with type 2 diabetes receiving oral antidiabetes agents	Cross over
<b>lispro vs glargine once-daily</b>			
<b>APOLLO (Bretzel) , 2008</b> [NCT00311818] n=NA follow-up:	nsulin lispro administered three times per day versus insulin glargine taken once daily at the same time every day	type 2 diabetes mellitus that was inadequately controlled by oral hypoglycaemic agents	
<b>insulin lispro protamine suspension plus lispro vs glargine plus lispro</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
Koivisto , 2011 n=NA	-	-	
<b>lispro vs insulin detemir</b>			
Fogelfeld , 2010 n=223/219 follow-up: 24 week	Insulin lispro protamine suspension versus insulin detemir once daily at bedtime	insulin-naive patients with Type 2 diabetes	Parallel groups open-label
<b>lispro + NPH vs NPH + SU</b>			
Bastyr , 1999 n=NA follow-up:	preprandial insulin lispro plus bedtime NPH insulin versus bedtime neutral protamine Hagedorn (NPH) insulin plus sulfonylurea	-	
<b>lispro insulin vs NPH insulin</b>			
Bastyr , 2000 n=NA follow-up:	insulin lispro versus bedtime NPH insulin	-	
<b>lispro + NPH vs NPH twice daily</b>			
Ceriello , 2007 n=NA follow-up: 12 weeks	premeal insulin lispro+bedtime neutral protamine Hagedorn (NPH) versus twice-daily NPH	patients with type 2 diabetes treated by a 2-month lead-in with twice-daily NPH treatment	Cross over open-label
<b>lispro insulin + NPH insulin vs regular insulin + NPH insulin</b>			
Altuntas , 2003 n=NA follow-up:	lispro insulin + NPH insulin versus regular insulin + NPH insulin	-	
<b>lispro twice daily + NPH insulin vs regular insulin + NPH insulin</b>			
Vignati n=NA follow-up:	twice-daily insulin lispro in combination with NPH human insulin versus regular human insulin in combination with NPH human insulin	-	

More details and results :

- intensive therapy for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q459>
- insulin therapy for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q548>

## References

### **Raz, 2009:**

Raz I, Wilson PW, Strojek K, Kowalska I, Bozikov V, Gitt AK, Jermendy G, Campaigne BN, Kerr L, Milicevic Z, Jacober SJ, Effects of prandial versus fasting glycemia on cardiovascular outcomes in type 2 diabetes: the HEART2D trial. *Diabetes Care* 2009;32:381-6. [[19246588](#)] [10.2337/dc08-1671](#)

### **Masuda, 2008:**

Masuda H, Sakamoto M, Irie J, Kitaoka A, Shiono K, Inoue G, Atsuda K, Yamada S, Comparison of twice-daily injections of biphasic insulin lispro and basal-bolus therapy: glycaemic control and quality-of-life of insulin-naive type 2 diabetic patients. *Diabetes Obes Metab* 2008;10:1261-5. [[18494811](#)] [10.1111/j.1463-1326.2008.00897.x](#)

### **Herman, 2005:**

Herman WH, Ilag LL, Johnson SL, Martin CL, Sinding J, Al Harthi A, Plunkett CD, LaPorte FB, Burke R, Brown MB, Halter JB, Raskin P A clinical trial of continuous subcutaneous insulin infusion versus multiple daily injections in older adults with type 2 diabetes. *Diabetes Care* 2005;28:1568-73 [[15983302](#)]

### **Strojek, 2010:**

Strojek K, Shi C, Carey MA, Jacober SJ, Addition of insulin lispro protamine suspension or insulin glargine to oral type 2 diabetes regimens: a randomized trial. *Diabetes Obes Metab* 2010;12:916-22. [[20920045](#)] [10.1111/j.1463-1326.2010.01257.x](#)

### **Chan META-ANALYSIS, 2009:**

Chan JY, Leyk M, Frier BM, Tan MH, Relationship between HbA1c and hypoglycaemia in patients with type 2 diabetes treated with different insulin regimens in combination with metformin. *Diabetes Metab Res Rev* 2009;25:224-31. [[19156705](#)] [10.1002/dmrr.929](#)

### **Robbins, 2007:**

Robbins DC, Beisswenger PJ, Ceriello A, Goldberg RB, Moses RG, Pagkalos EM, Milicevic Z, Jones CA, Sarwat S, Tan MH Mealtime 50/50 basal + prandial insulin analogue mixture with a basal insulin analogue, both plus metformin, in the achievement of target HbA1c and pre- and postprandial blood glucose levels in patients with type 2 diabetes: a multinational, 24-week, randomized, open-label, parallel-group comparison. *Clin Ther* 2007;29:2349-64 [[18158076](#)] [10.1016/j.clinthera.2007.11.016](#)

Robbins DC, Beisswenger PJ, Ceriello A, et al. Thrice-daily lispro mid mixture plus metformin improved glycemic control better than glargine plus metformin in patients with type 2 diabetes. *Diabetes*. 2006;55(Suppl 1 ):554-P. A132. Abstract

### **Kazda, 2006:**

Kazda C, Hlstrunk H, Helsberg K, Langer F, Forst T, Hanefeld M, Prandial insulin substitution with insulin lispro or insulin lispro mid mixture vs. basal therapy with insulin glargine: a randomized controlled trial in patients with type 2 diabetes beginning insulin therapy. *J Diabetes Complications* ;20:145-52. [[16632233](#)] [10.1016/j.jdiacomp.2005.09.004](#)

### **DURABLE (Buse) DOUBLONS, 2011:**

### **DURABLE (Buse), 2009:**

Buse JB, Wolffenbittel BH, Herman WH, Hippler S, Martin SA, Jiang HH, Shenouda SK, Fahrback JL, The DURABILITY of Basal versus Lispro mix 75/25 insulin Efficacy (DURABLE) trial: comparing the durability of lispro mix 75/25 and glargine. *Diabetes Care* 2011;34:249-55. [[21270182](#)] [10.2337/dc10-1701](#)

Miser WF, Arakaki R, Jiang H, Scism-Bacon J, Anderson PW, Fahrback JL, Randomized, open-label, parallel-group evaluations of basal-bolus therapy versus insulin lispro premixed therapy in patients with type 2 diabetes mellitus failing to achieve control with starter insulin treatment and continuing oral antihyperglycemic drugs: a noninferiority intensification substudy of the DURABLE trial. *Clin Ther* 2010;32:896-908. [[20685497](#)] [10.1016/j.clinthera.2010.05.001](#)

Wolffenbittel BH, Klaff LJ, Bhushan R, Fahrback JL, Jiang H, Martin S, Initiating insulin therapy in elderly patients with Type 2 diabetes: efficacy and safety of lispro mix 25 vs. basal insulin combined with oral glucose-lowering agents. *Diabet Med* 2009;26:1147-55. [[19929994](#)] [10.1111/j.1464-5491.2009.02824.x](#)

Buse JB, Wolffenbittel BH, Herman WH, Shemonsky NK, Jiang HH, Fahrbach JL, Scism-Bacon JL, Martin SA, DURAbility of basal versus lispro mix 75/25 insulin efficacy (DURABLE) trial 24-week results: safety and efficacy of insulin lispro mix 75/25 versus insulin glargine added to oral antihyperglycemic drugs in patients with type 2 diabetes. *Diabetes Care* 2009;32:1007-13. [19336625] [10.2337/dc08-2117](#)

Buse JB, Wolffenbittel BH, Herman WH, Shemonsky NK, Jiang HH, Fahrbach JL, Scism-Bacon JL, Martin SA, DURAbility of basal versus lispro mix 75/25 insulin efficacy (DURABLE) trial 24-week results: safety and efficacy of insulin lispro mix 75/25 versus insulin glargine added to oral antihyperglycemic drugs in patients with type 2 diabetes. *Diabetes Care* 2009;32:1007-13. [19336625] [10.2337/dc08-2117](#)

Fahrbach J, Jacober S, Jiang H, Martin S The DURABLE trial study design: comparing the safety, efficacy, and durability of insulin glargine to insulin lispro mix 75/25 added to oral antihyperglycemic agents in patients with type 2 diabetes. *J Diabetes Sci Technol* 2008 Sep;2:831-8 [19885269]

**Malone, 2004:**

Malone JK, Kerr LF, Campaigne BN, Sachson RA, Holcombe JH, , Combined therapy with insulin lispro Mix 75/25 plus metformin or insulin glargine plus metformin: a 16-week, randomized, open-label, crossover study in patients with type 2 diabetes beginning insulin therapy. *Clin Ther* 2004;26:2034-44. [15823767] [10.1016/j.clinthera.2004.12.015](#)

**Malone, 2005:**

Malone JK, Bai S, Campaigne BN, Reviriego J, Augendre-Ferrante B, Twice-daily pre-mixed insulin rather than basal insulin therapy alone results in better overall glycaemic control in patients with Type 2 diabetes. *Diabet Med* 2005;22:374-81. [15787659] [10.1111/j.1464-5491.2005.01511.x](#)

**Jacober, 2006:**

Jacober SJ, Scism-Bacon JL, Zagar AJ A comparison of intensive mixture therapy with basal insulin therapy in insulin-naive patients with type 2 diabetes receiving oral antidiabetes agents. *Diabetes Obes Metab* 2006;8:448-55 [16776752] [10.1111/j.1463-1326.2006.00605.x](#)

**APOLLO (Bretzel), 2008:**

Bretzel RG, Nuber U, Landgraf W, Owens DR, Bradley C, Linn T, Once-daily basal insulin glargine versus thrice-daily prandial insulin lispro in people with type 2 diabetes on oral hypoglycaemic agents (APOLLO): an open randomised controlled trial. *Lancet* 2008;371:1073-84. [18374840] [10.1016/S0140-6736\(08\)60485-7](#)

**Koivisto, 2011:**

Koivisto V, Cleall S, Pontiroli AE, Giugliano D, Comparison of insulin lispro protamine suspension versus insulin glargine once daily in basal-bolus therapies with insulin lispro in type 2 diabetes patients: a prospective randomized open-label trial. *Diabetes Obes Metab* 2011;13:1149-57. [21819517] [10.1111/j.1463-1326.2011.01484.x](#)

**Fogelfeld, 2010:**

Fogelfeld L, Dharmalingam M, Robling K, Jones C, Swanson D, Jacober S, A randomized, treat-to-target trial comparing insulin lispro protamine suspension and insulin detemir in insulin-naive patients with Type 2 diabetes. *Diabet Med* 2010;27:181-8. [20546262] [10.1111/j.1464-5491.2009.02899.x](#)

**Bastyr, 1999:**

Bastyr EJ, Johnson ME, Trautmann ME, Anderson JH, Vignati L, Insulin lispro in the treatment of patients with type 2 diabetes mellitus after oral agent failure. *Clin Ther* 1999;21:1703-14. [10566566]

**Bastyr, 2000:**

Bastyr EJ, Stuart CA, Brodows RG, Schwartz S, Graf CJ, Zagar A, Robertson KE, Therapy focused on lowering postprandial glucose, not fasting glucose, may be superior for lowering HbA1c. IOEZ Study Group. *Diabetes Care* 2000;23:1236-41. [10977012]

**Ceriello, 2007:**

Ceriello A, Del Prato S, Bue-Valleskey J, Beattie S, Gates J, de la Pea A, Malone J, Premeal insulin lispro plus bedtime NPH or twice-daily NPH in patients with type 2 diabetes: acute postprandial and chronic effects on glycemic control and cardiovascular risk factors. *J Diabetes Complications* ;21:20-7. [17189870]

[10.1016/j.jdiacomp.2005.11.005](https://doi.org/10.1016/j.jdiacomp.2005.11.005)

**Altuntas, 2003:**

Altuntas Y, Ozen B, Ozturk B, Sengul A, Ucak S, Ersoy O, Karul S, Comparison of additional metformin or NPH insulin to mealtime insulin lispro therapy with mealtime human insulin therapy in secondary OAD failure. *Diabetes Obes Metab* 2003;5:371-8. [[14617222](#)]

**Vignati, 0:**

Vignati L, Anderson JH, Iversen PW, Efficacy of insulin lispro in combination with NPH human insulin twice per day in patients with insulin-dependent or non-insulin-dependent diabetes mellitus. Multicenter Insulin Lispro Study Group. *Clin Ther* ;19:1408-21. [[9444449](#)]