

# Clinical trials of antidiabetic drugs for diabetes type 2 in patients with insufficient glycaemic control with bitherapy

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

## 1 DPP-4 inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>sitagliptin vs placebo (on-top glimepiride +/- metformine)</b>			
<b>Hermansen , 2007</b> n=NA follow-up:	sitagliptin 100 mg daily (add-on to ongoing stable doses of glimepiride, alone or in combination with metformin)ocumen versus placebo (add-on to ongoing stable doses of glimepiride, alone or in combination with metformin);	-	

## References

### Hermansen, 2007:

← Hermansen K, Kipnes M, Luo E, Fanurik D, Khatami H, Stein P Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, in patients with type 2 diabetes mellitus inadequately controlled on glimepiride alone or on glimepiride and metformin. Diabetes Obes Metab 2007;9:733-45 [[17593236](#)] [10.1111/j.1463-1326.2007.00744.x](https://doi.org/10.1111/j.1463-1326.2007.00744.x)

## 2 DPP-4 inhibitors add on MET+SU

Trial	Treatments	Patients	Trials design and methods
<b>linagliptin vs Metformin + sulfonylurea</b>			
<b>Owens</b> [NCT00602472] n=NA follow-up: 24 weeks	linagliptin versus combination of metformin and an SU	type 2 diabetes mellitus with insufficient glycaemic control with metformin in combination with a sulphonylurea	Argentina

## References

### Owens, 0:

Owens DR, Swallow R, Woerle HJ, et al. Linagliptin improves glycemic control in Type 2 diabetes patients inadequately controlled by metformin and sulfonylurea without weight gain and low risk of hypoglycaemia. Poster no 548-P, 70th American Diabetes Association Scientific Sessions, June 2010, Orlando, Florida U.S.A.

Owens DR, Swallow R, Dugi KA, Woerle HJ Efficacy and safety of linagliptin in persons with type 2 diabetes inadequately controlled by a combination of metformin and sulphonylurea: a 24-week randomized study. Diabet Med 2011;28:1352-61 [[21781152](#)] [10.1111/j.1464-5491.2011.03387.x](https://doi.org/10.1111/j.1464-5491.2011.03387.x)

### 3 DPP-4 inhibitors add on MET+TZD

Trial	Treatments	Patients	Trials design and methods
<b>linagliptin vs placebo (add on MET+TZD)</b>			
linagliptin 1218.61 <i>ongoing</i> [NCT00996658] n=NA follow-up:	Linagliptin (5 mg once daily) versus placebo (add on therapy to metformin in combination with pioglitazone)	Type 2 Diabetic Patients With Inadequate Glycaemic Control on Metformin in Combination With Pioglitazone	

### References

linagliptin 1218.61, 0:

### 4 glucagon-like peptide analogs

Trial	Treatments	Patients	Trials design and methods
<b>taspoglutide vs placebo</b>			
BC20963 <i>ongoing</i> [NCT00744367] n=NA follow-up: 24 weeks	taspoglutide 10mg once weekly, taspoglutide 20 mg once weekly (after 4 weeks of taspoglutide 10 mg once weekly) versus placebo in addition to their continued stable metformin plus pioglitazone treatment	patients with type 2 diabetes mellitus inadequately controlled with metformin plus pioglitazone	double-blind USA
<b>exenatide other doses vs placebo (add on MER+/-SU)</b>			
Fineman , 2003 n=109 follow-up: 28 days	exenatide 3 regimen (0.08 micro g/kg) for 28 days versus placebo	patients with tyep 2 diabetes treated with diet and a sulfonylurea and/or metformin	Parallel groups double-blind USA
<b>exenatide 20g/d vs placebo (add on MET+/-SU)</b>			
Gao , 2009 [NCT00324363] n=234/232 follow-up: 16 weeks	exenatide 5 mg then 10 mg twice-daily for 4 and 12 weeks versus placebo	Asian descent with type 2 diabetes and inadequate glycemic control taking metformin alone or Met and sulfonylureas	Parallel groups double-blind 4 countries
<b>exenatide 10g/d vs placebo (add on SU+/-MET/TZD)</b>			
Kadowaki (trial 8683) , 2009 n=111/40 follow-up: 12 weeks	Exenatide 10g daily for 12 weeks versus Placebo on-top of sulphonylureas +/-metformin/thiazolidinediones	Japanese patients with type 2 diabetes suboptimally controlled despite therapeutic dose of sulfonylurea, SU+biguanide or SU+thiazolidinedione	Parallel groups open Japan
<b>exenatide 10g/d vs placebo (add on SU+MET)</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Kendall 10g/d , 2005</b> [NCT00035984] n=245/247 follow-up: 30 weeks	Exenatide 5 g bid versus Placebo on-top of sulphonylureas+metformin	patients with type 2 diabetes unable to achieve glycemic control with metformin-sulfonylurea combination therapy	Parallel groups double blind USA
<b>exenatide 20g/d vs placebo (add on SU+MET)</b>			
<b>Kendall 20g/d , 2005</b> [NCT00035984] n=241/247 follow-up: 30 weeks	Exenatide 10 g bid versus Placebo on-top of sulphonylureas+metformin	patients with type 2 diabetes unable to achieve glycemic control with metformin-sulfonylurea combination therapy	Parallel groups double blind USA
<b>exenatide 20g/d vs placebo (add on TZD+/-MET)</b>			
<b>Zinman 20g/j , 2007</b> [NCT00099320] n=121/112 follow-up: 16 weeks	Exenatide 20 g daily versus Placebo on-top of thiazolidinediones+/-metformin	patients with type 2 diabetes that was suboptimally controlled with TZD treatment (with or without metformin)	double blind Canada, Spain, and the United States
<b>Zinman 20g/j A MODIFIER , 2007</b> n=121/112 follow-up: 16 weeks	exenatide Subcutaneous abdominal injections of 10 microg twice daily versus placebo	patients with type 2 diabetes that was suboptimally controlled with TZD treatment (with or without metformin)	Parallel groups double-blind Canada, Spain, and the United States
<b>liraglutide 1.2mg vs placebo (add on TZD+MET)</b>			
<b>LEAD-4 (1.2mg) , 2009</b> [NCT00333151] n=178/177 follow-up: 26 weeks	Liraglutide 1.2 daily versus Placebo on-top of thiazolidinediones + metformin	patients with type 2 diabetes, A1C 711% (previous OAD monotherapy >=3 months) or 710% (previous OAD combination therapy >=3 months), and BMI 45 kg/m2	Parallel groups double-blind USA, Canada
<b>liraglutide 1.8mg vs placebo (add on TZD+MET)</b>			
<b>LEAD-4 (1.8mg) , 2009</b> [NCT00333151] n=178/177 follow-up: 26 weeks	Liraglutide 1.8 daily versus Placebo on-top of thiazolidinediones + metformin	patients with type 2 diabetes, A1C 711% (previous OAD monotherapy >=3 months) or 710% (previous OAD combination therapy >=3 months), and BMI 45 kg/m2	double-blind USA, Canada
<b>exenatide once monthly vs weekly exenatide</b>			
<b>phase 2 exenatide once monthly unpublished</b> n=121 follow-up: 20 weeks	exenatide once monthly at a low, medium or high dose, each administered once every four weeks, for a total of 20 weeks versus exenatide 2mg once weekly	adults with type 2 diabetes who were not achieving adequate glucose control using diet and exercise alone or with a stable regimen of metformin, pioglitazone, or both	Parallel groups open
<b>taspoglutide vs exenatide</b>			
<b>BC21625 ongoing</b> [NCT00717457] n=NA follow-up:	taspoglutide versus exenatide	patients with type 2 diabetes mellitus inadequately controlled with metformin, thiazolidinedione or a combination of both	parallel groups open USA
<b>liraglutide 1.8mg vs exenatide on top MET/SU/MET+SU</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>LEAD-6 , 2009</b> [NCT00518882] n=233/231 follow-up: 26 weeks	liraglutide 1.8 mg once a day versus exenatide 10 microg twice a day	Adults with inadequately controlled type 2 diabetes on maximally tolerated doses of metformin, sulphonylurea, or both	Parallel groups open 15 countries
<b>exenatide 20g/d vs insulin (add on SU+MET)</b>			
<b>Heine , 2005</b> n=282/267 follow-up: 26 weeks	Exenatide 20 g daily versus Insulin on-top of sulphonylureas+metformin	-	open
<b>exenatide 20g/d vs insulin (add on SU/MET)</b>			
<b>Davis , 2007</b> [NCT00099333] n=33/16 follow-up: 16 weeks	Exenatide 20 g daily versus Insulin on-top of sulphonylureas/metformin	patients with type 2 diabetes using insulin in combination with oral antidiabetes agents	Parallel groups open USA
<b>exenatide 20g/d vs insulin BIAsp twice daily add on SU+MET</b>			
<b>Nauck , 2007</b> [NCT00082407] n=253/248 follow-up: 52 weeks	Exenatide 20 g daily versus Insulin on-top of sulphonylureas+metformin	patients with type 2 diabetes who were suboptimally controlled with sulfonylurea and metformin	Parallel groups open 13 countries
<b>taspoglutide vs insulin glargine</b>			
<b>ZC22565 ongoing</b> [NCT01051011] n=NA follow-up:	taspoglutide 10mg subcutaneously (sc) weekly, or taspoglutide 10mg sc weekly for 4 weeks followed by 20mg sc weekly versus insulin glargine at an initial dose of 10 international units sc daily	insulin-naive patients with type 2 diabetes mellitus inadequately controlled on merformin and sulfonylurea combination therapy	parallel groups open China
<b>taspoglutide vs insulin glargine (add on MET)</b>			
<b>BC20965 ongoing</b> [NCT00755287] n=NA follow-up: 2 years	taspoglutide (10 mg once weekly, or 10mg once weekly for 4 weeks followed by 20mg once weekly) versus insulin glargine (starting dose 10 IU/day) in addition to continued prestudy metformin treatment	patients with insulin-naive type 2 diabetes mellitus inadequately controlled with metformin and sulphonylurea combination therapy	open USA
<b>taspoglutide vs pioglitazone</b>			
<b>BC21893 ongoing</b> [NCT00909597] n=NA follow-up: 24 months	taspoglutide 10mg sc weekly, or taspoglutide 20mg sc weekly after 4 weeks of taspoglutide 10mg sc weekly versus pioglitazone 45mg/day po after 4 weeks of pioglitazone 30mg/day po	patients with type 2 diabetes mellitus inadequately controlled with sulfonylurea monotherapy or sulfonylurea plus metformin combination therapy	parallel groups double-blind USA

## References

**BC20963, 0:**

**Fineman, 2003:**

Fineman MS, Bicsak TA, Shen LZ, Taylor K, Gaines E, Varns A, Kim D, Baron AD Effect on glycemic control of exenatide (synthetic exendin-4) additive to existing metformin

and/or sulfonylurea treatment in patients with type 2 diabetes. *Diabetes Care* 2003;26:2370-7 [[12882864](#)]

**Gao, 2009:**

Gao Y, Yoon KH, Chuang LM, Mohan V, Ning G, Shah S, Jang HC, Wu TJ, Johns D, Northrup J, Brodows R Efficacy and safety of exenatide in patients of Asian descent with type 2 diabetes inadequately controlled with metformin or metformin and a sulphonylurea. *Diabetes Res Clin Pract* 2009;83:69-76 [[19019476](#)] [10.1016/j.diabres.2008.09.037](#)

**Kadowaki (trial 8683), 2009:**

Kadowaki T, Namba M, Yamamura A, Sowa H, Wolka AM, Brodows RG Exenatide exhibits dose-dependent effects on glycemic control over 12 weeks in Japanese patients with suboptimally controlled type 2 diabetes. *Endocr J* 2009;56:415-24 [[19194050](#)]

**Kendall 10g/d, 2005:**

Kendall DM, Riddle MC, Rosenstock J, Zhuang D, Kim DD, Fineman MS, Baron AD Effects of exenatide (exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. *Diabetes Care* 2005;28:1083-91 [[15855571](#)]

**Kendall 20g/d, 2005:**

Kendall DM, Riddle MC, Rosenstock J, Zhuang D, Kim DD, Fineman MS, Baron AD Effects of exenatide (exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. *Diabetes Care* 2005;28:1083-91 [[15855571](#)]

**Zinman 20g/j, 2007:**

Zinman B, Hoogwerf BJ, Durn Garca S, Milton DR, Giaconia JM, Kim DD, Trautmann ME, Brodows RG The effect of adding exenatide to a thiazolidinedione in suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2007;146:477-85 [[17404349](#)]

**Zinman 20g/j A MODIFIER, 2007:**

Zinman B, Hoogwerf BJ, Durn Garca S, Milton DR, Giaconia JM, Kim DD, Trautmann ME, Brodows RG The effect of adding exenatide to a thiazolidinedione in suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2007;146:477-85 [[17404349](#)]

**LEAD-4 (1.2mg), 2009:**

Zinman B, Gerich J, Buse JB, Lewin A, Schwartz S, Raskin P, Hale PM, Zdravkovic M, Blonde L, Efficacy and safety of the human glucagon-like peptide-1 analog liraglutide in combination with metformin and thiazolidinedione in patients with type 2 diabetes (LEAD-4 Met+TZD). *Diabetes Care* 2009;32:1224-30. [[19289857](#)] [10.2337/dc08-2124](#)

**LEAD-4 (1.8mg), 2009:**

Zinman B, Gerich J, Buse JB, Lewin A, Schwartz S, Raskin P, Hale PM, Zdravkovic M, Blonde L, Efficacy and safety of the human glucagon-like peptide-1 analog liraglutide in combination with metformin and thiazolidinedione in patients with type 2 diabetes (LEAD-4 Met+TZD). *Diabetes Care* 2009;32:1224-30. [[19289857](#)] [10.2337/dc08-2124](#)

**phase 2 exenatide once monthly, :**

**BC21625, 0:**

**LEAD-6, 2009:**

Buse JB, Rosenstock J, Sesti G, Schmidt WE, Montanya E, Brett JH, Zychma M, Blonde L Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). *Lancet* 2009 Jul 4;374:39-47 [[19515413](#)] [10.1016/S0140-6736\(09\)60659-0](#)

Buse JB, Sesti G, Schmidt WE, Montanya E, Chang CT, Xu Y, Blonde L, Rosenstock J Switching to once-daily liraglutide from twice-daily exenatide further improves glycemic control in patients with type 2 diabetes using oral agents. *Diabetes Care* 2010;33:1300-3 [[20332351](#)] [10.2337/dc09-2260](#)

Schmidt WE, Christiansen JS, Hammer M, Zychma MJ, Buse JB Patient-reported outcomes are superior in patients with Type?2 diabetes treated with liraglutide as compared with exenatide, when added to metformin, sulphonylurea or both: results from a randomized, open-label study. *Diabet Med* 2011 Mar 9;: [[21388442](#)] [10.1111/j.1464-5491.2011.03276.x](#)

**Heine, 2005:**

Heine RJ, Van Gaal LF, Johns D, Mihm MJ, Widel MH, Brodows RG Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2005;143:559-69 [[16230722](#)]

**Davis, 2007:**

Davis SN, Johns D, Maggs D, Xu H, Northrup JH, Brodows RG Exploring the substitution of exenatide for insulin in patients with type 2 diabetes treated with insulin in combination with oral antidiabetes agents. *Diabetes Care* 2007;30:2767-72 [[17595353](#)] [10.2337/dc06-2532](#)

**Nauck, 2007:**

Nauck MA, Duran S, Kim D, Johns D, Northrup J, Festa A, Brodows R, Trautmann M A comparison of twice-daily exenatide and biphasic insulin aspart in patients with type 2 diabetes who were suboptimally controlled with sulfonylurea and metformin: a non-inferiority study. *Diabetologia* 2007;50:259-67 [[17160407](#)] [10.1007/s00125-006-0510-2](#)

**ZC22565, 0:**

**BC20965, 0:**

**BC21893, 0:**

## 5 lixisenatide

Trial	Treatments	Patients	Trials design and methods
<b>lixisenatide vs placebo (add on basal insulin)</b>			
<b>GetGoal Duo1</b> <i>ongoing</i> [NCT00975286] n=NA follow-up: 24 weeks	Lixisenatide as an add-on treatment to insulin glargine and metformin versus placebo	patients with type 2 diabetes insufficiently controlled with insulin glargine and metformin	Parallel groups double-blind USA
<b>lixisenatide vs placebo (add on MET+/-SU)</b>			
<b>GetGoal-M-As</b> <i>ongoing</i> [NCT01169779] n=NA follow-up: 24 weeks	Lixisenatide (Titration phase: 10 g maintenance phase: 20 g, add-on treatment to metformin with or without sulfonylurea versus add-on treatment to metformin with or without sulfonylurea	-	double-blind China
<b>lixisenatide vs placebo (add on SU+/-MET)</b>			
<b>GETGOAL-S</b> <i>ongoing</i> [NCT00713830] n=NA follow-up: 24 weeks	AVE0010 in association with sulfonylurea without or with metformin versus placebo	patients with type 2 diabetes not adequately controlled with sulfonylurea	double-blind USA
<b>lixisenatide vs placebo (add on TZD+/-MET)</b>			
<b>GETGOAL-P</b> <i>ongoing</i> [NCT00763815] n=NA follow-up: 24 weeks	AVE0010 in association with pioglitazone with or without metformin versus placebo	Type 2 diabetes mellitus insufficiently controlled with pioglitazone with or without metformin	Parallel groups double-blind USA

## References

**GetGoal Duo1, 0:**

[10.2337/dc12-2462](#)

**GetGoal-M-As, 0:**

**GETGOAL-S, 0:**

**GETGOAL-P, 0:**

## 6 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.