

# Clinical trials of glucose lowering for cardiovascular prevention for diabetes type 2 in all type of patients

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

## 1 acarbose

Trial	Treatments	Patients	Trials design and methods
<b>acarbose vs placebo</b>			
<b>ACE</b> <i>ongoing</i> [NCT00829660] n=NA follow-up:	acarbose versus placebo	patients with impaired glucose tolerance who have established coronary heart disease or acute coronary syndrome	Parallel groups double-blind

## References

ACE, :

## 2 DPP-4 inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>linagliptin vs glimepiride</b>			
<b>CAROLINA</b> , 2012 [NCT01243424] n=776/775 follow-up: 2 years	linagliptin versus glimepiride 1-4 mg QD	patients with type 2 diabetes at elevated cardiovascular risk receiving usual care	double-blind USA
<b>alogliptin vs placebo</b>			
<b>EXAMINE</b> , 2013 [NCT00968708] n=2701/2679 follow-up: 1.5 years (median)	alogliptin versus placebo	patients with type 2 diabetes and either an acute myocardial infarction or unstable angina requiring hospitalization within the previous 15 to 90 days	Parallel groups double-blind
<b>linagliptin vs placebo</b>			
<b>CARMELINA</b> <i>ongoing</i> [NCT01897532] n=NA follow-up:	-	-	double-blind
<b>saxagliptin vs placebo</b>			
<b>SAVOR TIMI</b> , 2013 [NCT01107886] n=8280/8212 follow-up: 2.1 years (median)	saxagliptin versus placebo	patients with type 2 diabetes who had a history of, or were at risk for, cardiovascular events	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
<b>sitagliptin vs placebo</b>			
<b>TECOS , 2015</b> [NCT00790205] n=7332/7339 follow-up: 3.0 years (median)	sitagliptin phosphate, one 50 mg or one 100 mg tablet (dose dependant on renal function) orally, once daily versus placebo	patients with Type 2 Diabetes Mellitus having a history of cardiovascular disease and a hemoglobin A1c (HbA1c) of 6.5% to 8.0%	Parallel groups double-blind 38 countries

## References

### CAROLINA, 2012:

Gallwitz B, Rosenstock J, Rauch T, Bhattacharya S, Patel S, von Eynatten M, Dugi KA, Woerle HJ 2-year efficacy and safety of linagliptin compared with glimepiride in patients with type 2 diabetes inadequately controlled on metformin: a randomised, double-blind, non-inferiority trial. *Lancet* 2012 Aug 4;380:475-83 [22748821] [10.1016/S0140-6736\(12\)60691-6](https://doi.org/10.1016/S0140-6736(12)60691-6)

### EXAMINE, 2013:

White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GL, Perez AT, Fleck PR, Mehta CR, Kupfer S, Wilson C, Cushman WC, Zannad F Alogliptin after acute coronary syndrome in patients with type 2 diabetes. *N Engl J Med* 2013;369:1327-35 [23992602]

Kay S, Strickson A, Puelles J, Selby R, Benson E, Tolley K Comparative Effectiveness of Adding Alogliptin to Metformin Plus Sulfonylurea with Other DPP-4 Inhibitors in Type 2 Diabetes: A Systematic Review and Network Meta-Analysis. *Diabetes Ther* 2017;: [28275958]

### CARMELINA, :

### SAVOR TIMI, 2013:

Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med* 2013;369:1317-26 [23992601]

### TECOS, 2015:

Green JB, Bethel MA, Paul SK, Ring A, Kaufman KD, Shapiro DR, Califf RM, Holman RR Rationale, design, and organization of a randomized, controlled Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) in patients with type 2 diabetes and established cardiovascular disease. *Am Heart J* 2013;166:983-989.e7 [24268212]

Bethel MA, Green JB, Milton J, Tajar A, Engel SS, Califf RM, Holman RR Regional, age and sex differences in baseline characteristics of patients enrolled in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS). *Diabetes Obes Metab* 2015;17:395-402 [25600421]

Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, Josse R, Kaufman KD, Koglin J, Korn S, Lachin JM, McGuire DK, Pencina MJ, Standl E, Stein PP, Suryawanshi S, Van de Werf F, Peterson ED, Holman RR Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med* 2015 Jul 16;373:232-42 [26052984] [10.1056/NEJMoa1501352](https://doi.org/10.1056/NEJMoa1501352)

## 3 glucagon-like peptide 1 receptor agonist

Trial	Treatments	Patients	Trials design and methods
<b>dulaglutide vs placebo</b>			
<b>REWIND</b> <i>ongoing</i> [NCT01394952] n=NA follow-up:	-	-	
<b>exenatide vs placebo</b>			

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Trial	Treatments	Patients	Trials design and methods
<b>EXSCEL , 2017</b> [NCT01144338] n=7356/7396 follow-up: 3.2 years median	subcutaneous injections of extended-release exenatide at a dose of 2 mg once weakly versus placebo	patients with type 2 diabetes, with or without previous cardiovascular disease	Parallel groups double-blind
<b>liraglutide vs placebo</b>			
<b>LEADER , 2016</b> [NCT01179048] n=4668/4672 follow-up: 3.8 years (median)	Maximum dose of 1.8 mg liraglutide, injected subcutaneously once daily versus placebo	subjects with type 2 diabetes	double-blind Africa, Asia, Europe, North and South America
<b>lixisenatide vs placebo</b>			
<b>ELIXA</b> [NCT01147250] n=6068 follow-up: 25 months (median)	lixisenatide versus placebo	patients with T2DM and a recent ACS event	double-blind 49 countries
<b>semaglutide vs placebo</b>			
<b>SUSTAIN 6 , 2016</b> [NCT01720446] n=1648/1649 follow-up: 2.1 y (median)	once-weekly semaglutide (0.5 mg or 1.0 mg) versus placebo	patients with type 2 diabetes who were on a standardcare regimen	Parallel groups double-blind 20 countries
<b>tasoglutide vs placebo</b>			
<b>NCT01018173</b> <i>ongoing</i> [NCT01018173] n=NA	-	-	

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## References

### REWIND, :

### EXSCEL, 2017:

Holman RR, Bethel MA, Mentz RJ, Thompson VP, Lokhnygina Y, Buse JB, Chan JC, Choi J, Gustavson SM, Iqbal N, Maggioni AP, Marso SP, hman P, Pagidipati NJ, Poulter N, Ramachandran A, Zinman B, Hernandez AF Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med* 2017;: [28910237]

### LEADER, 2016:

Steinberg WM, Nauck MA, Zinman B, Daniels GH, Bergenstal RM, Mann JF, Steen Ravn L, Moses AC, Stockner M, Baeres FM, Marso SP, Buse JB LEADER 3–lipase and amylase activity in subjects with type 2 diabetes: baseline data from over 9000 subjects in the LEADER Trial. *Pancreas* 2014;43:1223-31 [25275271]

Petrie JR, Marso SP, Bain SC, Franek E, Jacob S, Masmiquel L, Leiter LA, Haluzik M, Satman I, Omar M, Shestakova M, Van Gaal L, Mann JF, Baeres FM, Zinman B, Poulter NR LEADER-4: blood pressure control in patients with type 2 diabetes and high cardiovascular risk: baseline data from the LEADER randomized trial. *J Hypertens* 2016;: [26855018]

Masmiquel L, Leiter LA, Vidal J, Bain S, Petrie J, Franek E, Raz I, Comlekci A, Jacob S, van Gaal L, Baeres FM, Marso SP, Eriksson M LEADER 5: prevalence and cardiometabolic impact of obesity in cardiovascular high-risk patients with type 2 diabetes mellitus: baseline global data from the LEADER trial. *Cardiovasc Diabetol* 2016;15:29 [26864124]

Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zinman B, Bergenstal RM, Buse JB Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med* 2016;: [27295427]

### ELIXA, :

Bentley-Lewis R, Aguilar D, Riddle MC, Claggett B, Diaz R, Dickstein K, Gerstein HC, Johnston P, Kber LV, Lawson F, Lewis EF, Maggioni AP, McMurray JJ, Ping L, Probstfield JL, Solomon SD, Tardif JC, Wu Y, Pfeffer MA Rationale, design, and baseline characteristics in Evaluation of LIXisenatide in Acute Coronary Syndrome, a long-term cardiovascular end point trial of lixisenatide versus placebo. *Am Heart J* 2015;169:631-638.e7 [25965710]

Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Kber LV, Lawson FC, Ping L, Wei X, Lewis EF, Maggioni AP, McMurray JJ, Probstfield JL, Riddle MC, Solomon SD, Tardif JC Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med 2015;373:2247-57 [26630143]

Pfeffer MA, Claggett B, Diaz R, Dickstein K, Gerstein HC, Kber LV, Lawson FC, Ping L, Wei X, Lewis EF, Maggioni AP, McMurray JJ, Probstfield JL, Riddle MC, Solomon SD, Tardif JC Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. N Engl J Med 2015;373:2247-57 [26630143]

#### SUSTAIN 6, 2016:

Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jdar E, Leiter LA, Lingvay I, Rosenstock J, Seufert J, Warren ML, Woo V, Hansen O, Holst AG, Pettersson J, Vilsbll T Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2016 Sep 15;: [27633186] 10.1056/NEJMoa1607141

NCT01018173, :

## 4 induced HbA1c reduction

Trial	Treatments	Patients	Trials design and methods
<b>metformin vs placebo</b>			
HOME , 2009 [NCT00375388] n=196/194 follow-up: 4.3 y	metformin 850 mg versus placebo	patients with DM2 treated with insulin	Parallel groups double-blind The Netherlands

### References

#### HOME, 2009:

Kooy A, de Jager J, Lehert P, Bets D, Wulfel MG, Donker AJ, Stehouwer CD Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. Arch Intern Med 2009;169:616-25 [19307526] 10.1001/archinternmed.2009.20

## 5 insulin

Trial	Treatments	Patients	Trials design and methods
<b>insulin glargine vs control</b>			
ORIGINE , 2012 [NCT00069784] n=6264/6273 follow-up: 6.2 years	insulin glargine (with a target fasting blood glucose level of 95 mg per deciliter versus standard care	with cardiovascular risk factors plus impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes	

### References

#### ORIGINE, 2012:

Gerstein HC, Bosch J, Dagenais GR, Daz R, Jung H, Maggioni AP, Pogue J, Probstfield J, Ramachandran A, Riddle MC, Rydn LE, Yusuf S Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012;367:319-28 [22686416]

## 6 PPAR modulator

Trial	Treatments	Patients	Trials design and methods
<b>aleglitazar vs placebo</b>			
<b>ALECARDIO , 2014</b> [NCT01042769] n=3616/3610 follow-up: 2 years ( median)	aleglitazar 150 g daily versus placebo	patients hospitalized for ACS (myocardial infarction or unstable angina) with type 2 diabetes	Parallel groups double-blind
<b>ALEPREVENT</b> [EUDRACT201200067116] n=1999 follow-up: 58 days	aleglitazar 150 g versus placebo	patients with T2D or prediabetes with established, stable CV disease	Parallel groups double-blind

## References

### ALECARDIO, 2014:

Lincoff AM, Tardif JC, Schwartz GG, Nicholls SJ, Rydn L, Neal B, Malmberg K, Wedel H, Buse JB, Henry RR, Weichert A, Cannata R, Svensson A, Volz D, Grobbee DE Effect of aloglitazar on cardiovascular outcomes after acute coronary syndrome in patients with type 2 diabetes mellitus: the AleCardio randomized clinical trial. JAMA 2014 Apr 16;311:1515-25 [24682069] [10.1001/jama.2014.3321](https://doi.org/10.1001/jama.2014.3321)

### ALEPREVENT, :

Erdmann E, Califf R, Gerstein HC, Malmberg K, Ruilope L, Schwartz GG, Wedel H, Volz D, Ditmarsch M, Svensson A, Bengus M Effects of the dual peroxisome proliferator-activated receptor activator aloglitazar in patients with Type 2 Diabetes mellitus or prediabetes. Am Heart J 2015;170:117-22 [26093872]

## 7 SGLT2 inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>canagliflozin vs placebo</b>			
<b>CANVAS , 2017</b> [NCT01032629] n=5795/4347 follow-up: 188.2 weeks (mean)	canagliflozin versus placebo	participants with type 2 diabetes and high cardiovascular risk	double-blind
<b>dapagliflozin vs placebo</b>			
<b>DECLARE TIMI 58</b> <i>ongoing</i> [NCT01730534] n=NA follow-up:	-	-	
<b>empagliflozin vs placebo</b>			
<b>EMPA-REG OUTCOME , 2015</b> [NCT01131676] n=4687/2333 follow-up: 3.1 years (median)	10 mg or 25 mg of empagliflozin once daily versus placebo	patients with type 2 diabetes at high cardiovascular risk	Parallel groups double-blind 42 countries

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Trial	Treatments	Patients	Trials design and methods
<b>ertugliflozin vs placebo</b>			
<b>VERTIS CV</b> <i>ongoing</i> [NCT01986881] n=8000 follow-up:	Ertugliflozin 15 mg and 5 mg versus placebo	participants with type 2 diabetes mellitus and established vascular disease	

## References

### CANVAS, 2017:

Neal B, Perkovic V, de Zeeuw D, Mahaffey KW, Fulcher G, Stein P, Desai M, Shaw W, Jiang J, Vercruysse F, Meininger G, Matthews D Rationale, design, and baseline characteristics of the Canagliflozin Cardiovascular Assessment Study (CANVAS)—a randomized placebo-controlled trial. *Am Heart J* 2013;166:217-223.e11 [23895803]

Fulcher G, Matthews DR, Perkovic V, de Zeeuw D, Mahaffey KW, Weiss R, Rosenstock J, Capuano G, Desai M, Shaw W, Vercruysse F, Meininger G, Neal B Efficacy and Safety of Canagliflozin Used in Conjunction with Sulfonylurea in Patients with Type 2 Diabetes Mellitus: A Randomized, Controlled Trial. *Diabetes Ther* 2015;6:289-302 [26081793]

Neal B, Perkovic V, de Zeeuw D, Mahaffey KW, Fulcher G, Ways K, Desai M, Shaw W, Capuano G, Alba M, Jiang J, Vercruysse F, Meininger G, Matthews D Efficacy and safety of canagliflozin, an inhibitor of sodium-glucose cotransporter 2, when used in conjunction with insulin therapy in patients with type 2 diabetes. *Diabetes Care* 2015;38:403-11 [25468945]

Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erond N, Shaw W, Law G, Desai M, Matthews DR Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med* 2017;; [28605608]

### DECLARE TIMI 58, :

### EMPA-REG OUTCOME, 2015:

Zinman B, Inzucchi SE, Lachin JM, Wanner C, Ferrari R, Fitchett D, Bluhmki E, Hantel S, Kempthorne-Rawson J, Newman J, Johansen OE, Woerle HJ, Broedl UC Rationale, design, and baseline characteristics of a randomized, placebo-controlled cardiovascular outcome trial of empagliflozin (EMPA-REG OUTCOME). *Cardiovasc Diabetol* 2014;13:102 [24943000]

Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med* 2015 Sep 17;; [26378978] 10.1056/NEJMoa1504720

### VERTIS CV, :

## 8 thiazolidinediones

Trial	Treatments	Patients	Trials design and methods
<b>rosiglitazone vs metformin/sulfonylurea</b>			
<b>RECORD , 2013</b> [NCT00379769] n=NA follow-up:	-	-	
<b>pioglitazone vs placebo</b>			
<b>IRIS , 2016</b> [NCT00091949] n=NA	-	-	

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Trial	Treatments	Patients	Trials design and methods
<b>PROACTIVE</b> [NCT00174993] n=2605/2633 follow-up: 34.5 months	oral pioglitazone titrated from 15 mg to 45 mg versus placebo	patients with type 2 diabetes who had evidence of macrovascular disease.	

## References

### RECORD, 2013:

Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJ Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. *Lancet* 2009 Jun 20;373:2125-35 [[19501900](#)]

Home PD, Pocock SJ, Beck-Nielsen H, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJ Rosiglitazone evaluated for cardiovascular outcomes—an interim analysis. *N Engl J Med* 2007 Jul 5;357:28-38 [[17551159](#)]

Mahaffey KW, Hafley G, Dickerson S, Burns S, Tourt-Uhlig S, White J, Newby LK, Komajda M, McMurray J, Bigelow R, Home PD, Lopes RD Results of a reevaluation of cardiovascular outcomes in the RECORD trial. *Am Heart J* 2013 Aug;166:240-249.e1 [[23895806](#)]

### IRIS, 2016:

Kernan WN, Viscoli CM, Furie KL, Young LH, Inzucchi SE, Gorman M, Guarino PD, Lovejoy AM, Peduzzi PN, Conwit R, Brass LM, Schwartz GG, Adams HP Jr, Berger L, Carolei A, Clark W, Coull B, Ford GA, Kleindorfer D, O'Leary JR, Parsons MW, Ringleb P, Sen S, Sp Pioglitazone after Ischemic Stroke or Transient Ischemic Attack. *N Engl J Med* 2016 Apr 7;374:1321-31 [[26886418](#)] [10.1056/NEJMoa1506930](#)

### PROACTIVE, :

Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefbvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Koryni L, Laakso M, Mokn M, Norkus A, Pirags V, Po Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. *Lancet* 2005;366:1279-89 [[16214598](#)]

## 9 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.