

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

TrialResults-center www.trialresultscenter.org

1 acarbose

Trial	Treatments	Patients	Trials design and methods
acarbose vs placebo			
ACE <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
linagliptin vs glimepiride			
CAROLINA , 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
alogliptin vs placebo			
EXAMINE , 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
linagliptin vs placebo			
CARMELINA <i>ongoing</i> [NCT01897532] n=NA follow-up:	-	-	double-blind
saxagliptin vs placebo			
SAVOR TIMI , 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
sitagliptin vs placebo			
TECOS , 2015 [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:

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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
dulaglutide vs placebo			
REWIND <i>ongoing</i> [NCT01394952] n=NA follow-up:	-	-	
exenatide vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
EXSCEL , 2017 [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
liraglutide vs placebo			
LEADER , 2016 [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
lixisenatide vs placebo			
ELIXA [NCT01147250] n=6068 follow-up: 25 months (median)	lixisenatide versus placebo	patients with T2DM and a recent ACS event	double-blind 49 countries
semaglutide vs placebo			
SUSTAIN 6 , 2016 [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
tasoglutide vs placebo			
NCT01018173 <i>ongoing</i> [NCT01018173] n=NA	-	-	

3

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]

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ELIXA, :

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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
metformin vs placebo			
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
insulin glargine vs control			
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
aleglitazar vs placebo			
ALECARDIO , 2014 [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
ALEPREVENT [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
canagliflozin vs placebo			
CANVAS , 2017 [NCT01032629] n=5795/4347 follow-up: 188.2 weeks (mean)	canagliflozin versus placebo	participants with type 2 diabetes and high cardiovascular risk	double-blind
dapagliflozin vs placebo			
DECLARE TIMI 58 , 2018 [NCT01730534] n=NA follow-up: approx 4 years (median)	-	adults with T2D at risk of CV events, including patients with multiple CV risk factors or established CV disease	double-blind
empagliflozin vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
EMPA-REG OUTCOME , 2015 [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
ertugliflozin vs placebo			
VERTIS CV <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, Vercruyse 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, Vercruyse 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](#)]

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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, 2018:

Wiviott SD The design and rationale for the Dapagliflozin Effect on Cardiovascular Events (DECLARE)-TIMI 58 Trial. *Am Heart J* 2018;200:83-89 [[29898853](#)] [10.1016/j.ahj.2018.01.012](#)

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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
rosiglitazone vs metformin/sulfonylurea			
RECORD , 2013 [NCT00379769] n=NA follow-up:	-	-	

continued...

Trial	Treatments	Patients	Trials design and methods
pioglitazone vs placebo			
IRIS , 2016 [NCT00091949] n=NA	-	-	
PROACTIVE [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.

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