

# Clinical trials of glucose lowering for cardiovascular prevention for diabetes type 2 in meta-regression

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

## 1 DPP-4 inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>linagliptin vs glimepiride</b>			
<b>CAROLINA , 2012</b> [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 , 2013</b> [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 ongoing</b> [NCT01897532] n=NA follow-up:	-	-	double-blind
<b>saxagliptin vs placebo</b>			
<b>SAVOR TIMI , 2013</b> [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
<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](#)

### 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 Sulfonyleurea 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

## 2 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>			
<b>EXSCEL</b> , 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
<b>liraglutide vs placebo</b>			
<b>LEADER</b> , 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
<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>			

continued...

Trial	Treatments	Patients	Trials design and methods
<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	-	-	

## 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, :

## 3 induced HbA1c reduction

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>metformin vs placebo</b>			
<b>HOME , 2009</b> [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
<b>tolbutamide or phenformin vs placebo</b>			
<b>UGDP (Tolb or Phen) , 1975</b> n=408/205 follow-up: >5 years	tolbutamide(1.5mg daily) or phenformin (100mg daily) versus placebo	patient with non insulin-dependent adult onset diabetes	double-blind
<b>glitazone vs conventional treatment</b>			
<b>PROactive , 2005</b> [NCT00174993] n=2605/2633 follow-up: 34.5 months	pioglitazone titrated 15-45 mg daily versus standard treatment	patients with type 2 diabetes who had evidence of macrovascular disease	Parallel groups double blind 19 countries
<b>intensive glycemc control vs conventional treatment</b>			
<b>UGDP (insulin) , 1982</b> n=204/210 follow-up: >5 years	intensive insulin versus standard insulin	patient with non insulin-dependent adult onset diabetes	Parallel groups open
<b>ACCORD , 2008</b> [NCT00000620] n=5128/5123 follow-up: 3.5y (5y)	very intensive glycemc control through currently available means (targetinga glycosylated hemoglobin <6% ) during a mean of 3.7 years versus standard glycemc control (targeting a glycosylated hemoglobin 7.0-7.9% )	patients with type 2 diabetes mellitus at high risk of death and stroke (pre-existing heart disease or two or more additional risk factors for heart disease)	Factorial plan open USA, Canada
<b>ADDITION , 2010</b> [NCT00237549] n=1678/1379 follow-up: 5 year	intensive multifactorial treatment versus routine care	patients with newly diagnosed type 2 diabetes	Parallel groups open Denmark, United Kingdom, the Netherlands
<b>ADVANCE , 2008</b> [NCT00145925] n=5571/5569 follow-up: median 5 y	intensive glucose-lowering treatments HbA1C <=6.5% using gliclazide(modified release) plus other drugs versus standard glucose-lowering treatments (targetglycated hemoglobin levels defined on the basisof local guidelines)	patients with type 2 diabetes	Parallel groups open 20 countries
<b>Kumamoto (primary prev) , 1995</b> n=28/27 follow-up: 8.0y	intensive glycemc control with multiple insulin injection treatment versus conventional insulin injection treatment (1-2 daily injections)	patients with non-insulin-dependent diabetes mellitus and with no retinopathy and urinary albumin excretions <30 mg/24 h	Parallel groups open Japan

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Kumamoto (secondary prev) , 1995</b> n=27/28 follow-up: 8.0y	multiple insulin injection treatment versus conventional insulin injection treatment (1-2 daily injections)	patients with non-insulin-dependent diabetes mellitus and simple retinopathy	Parallel groups open Japan
<b>Steno 2 , 2003</b> n=80/80 follow-up: 7.8 y	targeted, intensified, multifactorial intervention versus conventional treatment on modifiable risk factors for cardiovascular disease	patients with type 2 diabetes and microalbuminuria	Parallel groups open Denmark
<b>UKPDS 33 , 1998</b> n=2729/1138 follow-up: 10.3 y	intensive policy with a sulphonylurea (chlorpropamide, glibenclamide, or glipizide) or with insulin; fasting plasma glucose <6.0 mmol/L versus conventional policy with diet	newly diagnosed patients with type 2 diabetes who after 3 months diet treatment had a mean of two fasting plasma glucose concentrations of 61150 mmol/L	Parallel groups open UK
<b>VA CSDM , 1997</b> n=75/78 follow-up: 2.3y	intensive glycemic control (stepped plan from 1 evening injection of insulin, alone or with glipizide, to multiple daily injections, target to attain near-normal glycemia levels) versus standard treatment (1 insulin injection every morning)	non-insulin-dependent diabetes mellitus patients	Parallel groups open USA
<b>VADT , 2008</b> [NCT00032487] n=892/899 follow-up: 5.6y	intensive glucose control versus standard glucose control	military veterans who had a suboptimal response to therapy for type 2 diabetes	Parallel groups open US
<b>glitazone vs glimepiride</b>			
<b>PERISCOPE , 2008</b> [NCT00225277] n=274/273 follow-up: 18 months	pioglitazone 15 to 45 mg versus glimepiride, 1 to 4 mg	patients with coronary disease and type 2 diabetes	double blind North and South America
<b>glitazone vs glyburide</b>			
<b>Giles , 2008</b> [NCT00521820] n=262/256 follow-up: 6 months	pioglitazone for 6 months versus glyburide	patients with type 2 diabetes, systolic dysfunction, and NYHA functional Class II/III HF	Parallel groups open
<b>metformin vs glyburide</b>			
<b>ADOPT , 2006</b> [NCT00279045] n=1454/1441 follow-up: 4 years (median)	metformin, versus glyburide	recently diagnosed type 2 diabetes	Parallel groups

CT

## 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](https://doi.org/10.1001/archinternmed.2009.20)

### **UGDP (Tolb or Phen), 1975:**

The University Group Diabetes Program. A study of the effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes. V. Evaluation of pheniformin therapy. *Diabetes* 1975;24 Suppl 1:65-184 [[1090475](#)]

A study of the effects of hypoglycemia agents on vascular complications in patients with adult-onset diabetes. VI. Supplementary report on nonfatal events in patients treated with tolbutamide. *Diabetes* 1976;25:1129-53 [[992232](#)]

### **PROactive, 2005:**

Charbonnel B, Dormandy J, Erdmann E, Massi-Benedetti M, Skene A The prospective pioglitazone clinical trial in macrovascular events (PROactive): can pioglitazone reduce cardiovascular events in diabetes? Study design and baseline characteristics of 5238 patients. *Diabetes Care* 2004;27:1647-53 [[15220241](#)]

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, Koranyi 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](#)] [10.1016/S0140-6736\(05\)67528-9](#)

Wilcox R, Kupfer S, Erdmann E Effects of pioglitazone on major adverse cardiovascular events in high-risk patients with type 2 diabetes: results from PROspective pioglitAzone Clinical Trial In macro Vascular Events (PROactive 10). *Am Heart J* 2008;155:712-7 [[18371481](#)] [10.1016/j.ahj.2007.11.029](#)

### **UGDP (insulin), 1982:**

Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes. VIII. Evaluation of insulin therapy: final report. *Diabetes* 1982;31 Suppl 5:1-81 [[6757026](#)]

### **ACCORD, 2008:**

Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008;358:2545-59 [[18539917](#)]

Goff DC Jr, Gerstein HC, Ginsberg HN, Cushman WC, Margolis KL, Byington RP, Buse JB, Genuth S, Probstfield JL, Simons-Morton DG Prevention of cardiovascular disease in persons with type 2 diabetes mellitus: current knowledge and rationale for the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99:4i-20i [[17599424](#)]

Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes. *N Engl J Med* 2010 Jun 29;: [[20587587](#)] [10.1056/NEJMoa1001288](#)

Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, Cuddihy R, Cushman WC, Genuth S, Grimm RH Jr, Hamilton BP, Hoogwerf B, Karl D, Katz L, Krikorian A, O'Connor P, Pop-Busui R, Schubart U, Simmons D, Taylor H, Thomas A, Weiss D, Hramiak I Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. *Lancet* 2010 Jun 29;: [[20594588](#)] [10.1016/S0140-6736\(10\)60576-4](#)

Klein BE Reduction in Risk of Progression of Diabetic Retinopathy. *N Engl J Med* 2010 Jun 29;: [[20587586](#)] [10.1056/NEJMe1005667](#)

Gerstein HC, Miller ME, Genuth S, Ismail-Beigi F, Buse JB, Goff DC Jr, Probstfield JL, Cushman WC, Ginsberg HN, Bigger JT, Grimm RH Jr, Byington RP, Rosenberg YD, Friedewald WT Long-term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med* 2011 Mar 3;364:818-28 [[21366473](#)] [10.1056/NEJMoa1006524](#)

### **ADDITION, 2010:**

Sandbaek A, Griffin SJ, Rutten G, Davies M, Stolk R, Khunti K, Borch-Johnsen K, Wareham NJ, Lauritzen T Stepwise screening for diabetes identifies people with high but modifiable coronary heart disease risk. The ADDITION study. *Diabetologia* 2008;51:1127-34 [[18443762](#)] [10.1007/s00125-008-1013-0](#)

Griffin SJ, Borch-Johnsen K, Davies MJ, Khunti K, Rutten GE, Sandbk A, Sharp SJ, Simmons RK, van den Donk M, Wareham NJ, Lauritzen T Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet* 2011 Jun 24;: [[21705063](#)] [10.1016/S0140-6736\(11\)60698-3](#)

### **ADVANCE, 2008:**

Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, Marre M, Cooper M, Glasziou P, Grobbee D, Hamet P, Harrap S, Heller S, Liu L, Mancia G, Mogensen CE, Pan C, Poulter N, Rodgers A, Williams B, Bompont S, de Galan BE, Joshi R, Travert F Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2008;358:2560-72 [[18539916](#)]

### **Kumamoto (primary prev), 1995:**

Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995;28:103-17 [7587918]

**Kumamoto (secondary prev), 1995:**

Shichiri M, Kishikawa H, Ohkubo Y, Wake N Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. *Diabetes Care* 2000;23 Suppl 2:B21-9 [10860187]

Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995;28:103-17 [7587918]

**Steno 2, 2003:**

Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003;348:383-93 [12556541]

**UKPDS 33, 1998:**

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:837-53 [9742976]

**VA CSDM, 1997:**

Abraira C, Colwell J, Nuttall F, Sawin CT, Henderson W, Comstock JP, Emanuele NV, Levin SR, Pacold I, Lee HS Cardiovascular events and correlates in the Veterans Affairs Diabetes Feasibility Trial. Veterans Affairs Cooperative Study on Glycemic Control and Complications in Type II Diabetes. *Arch Intern Med* 1997;157:181-8 [9009975]

**VADT, 2008:**

Duckworth W, Abraira C, Moritz T, Reda D, Emanuele N, Reaven PD, Zieve FJ, Marks J, Davis SN, Hayward R, Warren SR, Goldman S, McCarren M, Vitek ME, Henderson WG, Huang GD Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes. *N Engl J Med* 2008 Dec 17;: [19092145]

**PERISCOPE, 2008:**

Nissen SE, Nicholls SJ, Wolski K, Nesto R, Kupfer S, Perez A, Jure H, De Laroche R, Staniloae CS, Mavromatis K, Saw J, Hu B, Lincoff AM, Tuzcu EM Comparison of pioglitazone vs glimepiride on progression of coronary atherosclerosis in patients with type 2 diabetes: the PERISCOPE randomized controlled trial. *JAMA* 2008 Apr 2;299:1561-73 [18378631]

**Giles, 2008:**

Giles TD, Miller AB, Elkayam U, Bhattacharya M, Perez A Pioglitazone and heart failure: results from a controlled study in patients with type 2 diabetes mellitus and systolic dysfunction. *J Card Fail* 2008;14:445-52 [18672190] 10.1016/j.cardfail.2008.02.007

**ADOPT, 2006:**

Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill MC, Zinman B, Viberti G Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. *N Engl J Med* 2006 Dec 7;355:2427-43 [17145742]

## 4 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](#)]

## 5 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](#)

### 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](#)]

## 6 SGLT2 inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>canagliflozin vs placebo</b>			
<b>CANVAS , 2017</b> [NCT01032629] n=5795/4347 follow-up:	-	-	
<b>dapagliflozin vs placebo</b>			

continued...



Trial	Treatments	Patients	Trials design and methods
<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
<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, :

## 7 thiazolidinediones

Trial	Treatments	Patients	Trials design and methods
<b>pioglitazone vs placebo</b>			

continued...



LMF CY-216, LMF CY 216, LMF CY216, , Furosemide, Frusemide, Fursemide, Frusemid, Furanthril, Furantral, Salix (brand of furosemide), Furosemide Monosodium Salt, Fusid, Lasix, Errolon, Furosemide Monohydrochloride, , Gemfibrozil, Gemfibrosil, Bolutol, CI-719, CI 719, CI719, DBL Gemfibrozil, Trialmin, Decrelip, Gemfi 1A Pharma, Gemfibrozilo Ur, Gemhexal, Gen-Gemfibrozil, Gen Gemfibrozil, GenGemfibrozil, GenRX Gemfibrozil, Healthsense Gemfibrozil, Jezil, Lipazil, Lipox Gemfi, Litarek, Lopid, Lopid R, Lipur, Pilder, SBPA Gemfibrozil, Apo-Gemfibrozil, Apo Gemfibrozil, ApoGemfibrozil, Ausgem, , Heparin, Unfractionated Heparin, Heparinic Acid, Liquaemin, Sodium Heparin, Heparin Sodium, alpha-Heparin, alpha Heparin, , Labetalol, Labetolol, Albetol, Apo-Labetalol, Apo Labetalol, ApoLabetalol, Dilevalol, Normodyne, Presolol, SCH-19927, SCH 19927, SCH19927, Trandate, AH-5158, AH 5158, AH5158, Labetalol Hydrochloride, , Nadroparine, Fraxiparin, Fraxiparine, CY 216, CY-216, CY216, LMF CY-216, LMF CY 216, LMF CY216, , Nicardipine, Cardene SR, Dagan, Flusemide, Lecibral, Lincil, Loxen, Lucenfal, Nicardipine Hydrochloride, Nicardipine LA, Nicardipino Ratiopharm, Nicardipino Seid, Perdipine, Ridene, Y-93, Y 93, Y93, Cardene I.V., Cardene, Vasonase, Antagonil, , Nicorandil, 2-Nicotinamidoethyl Nitrate, 2 Nicotinamidoethyl Nitrate, 2-Nicotinamidethyl Nitrate, 2 Nicotinamidethyl Nitrate, SG-75, SG 75, SG75, Ikorel, Adancor, Dancor, , Nifedipine, Adalat, Bay-1040, Bay 1040, Bay1040, BAY-a-1040, BAY a 1040, BAYa1040, Procardia XL, Nifedipine-GTIS, Nifedipine GTIS, Corinfar, Korinfar, Fenigidin, Nifangin, Nifedipine Monohydrochloride, Procardia, Vascard, Cordipin, Cordipine, , Nitroglycerin, Glyceryl Trinitrate, Nitrolan, Nitrostat, Perlinganit, Susadrin, Sustac, Sustak, Sustonit, Transderm Nitro, Tridil, Trinitrin, Trinitrolong, Anginine, Dynamite, Gilustenon, Nitrangin, Nitro-Bid, Nitro Bid, NitroBid, Nitro-Dur, Nitro Dur, NitroDur, Nitrocard, Nitroderm, Nitroderm TTS, Nitroglyn, Nitrol, Nitrong, Nitrospan, , omapatrilat, Vanlev, BMS 186716, BMS-186716, , Omacor, Lovaza, omega-3 ethyl ester 90, P-OM3 adjunct, , Logiparin, LHN-1, , orlistat, tetrahydrolipstatin, THLP, Alli, Xenical, , Pentoxifylline, Oxpentifylline, BL-191, BL 191, BL191, Trental, Torental, Agapurin, Pentoxil, , Perindopril, Pirindopril, Perstarium, S-9490, S 9490, S9490, S 9490-3, S 9490 3, S 94903, Perindopril Erbumine, , Actos, Practolol, ICI-50172, ICI 50172, ICI50172, Dalzic, Eralzdin Practolol, , Pravastatin, Eptastatin, Liplat, RMS-431, RMS 431, RMS431, SQ-31000, SQ 31000, SQ31000, Vasten, Bristacol, CS-514, CS 514, CS514, Lipemol, Praereduct, Mevalotin, Pravachol, Elisor, Selektine, Pravacol, Pravasin, Lipostat, , prasugrel, CS 747, CS-747, LY 640315, LY640315, LY-640315, Effient, Efient, Probuocol, DH-581, DH 581, DH581, Lorelco, Lurselle, Superlipid, Biphenabid, Panavir, , Propranolol, Propanolol, Avlocardyl, AY-20694, AY 20694, AY20694, Betadren, Dexpropranolol, Inderal, Obsidan, Obzidan, Propranolol Hydrochloride, Rexigen, Anaprilin, Anapriline, Dociton, , Triatec, Altace, Delix, Ramace, Vesdil, Carasel, Acovil, Tritace, Zabien, renolazine, RS 43285-193, Ranexa, RS 43285, RS-43285, , rimonabant, SR141716, SR 141716, Acomplia, Zimulti, SR 141716A, SR141716A, SR-141716A, , Xarelto, BAY 59-7939, , Avandia, Crestor, Tissue Plasminogen Activator, Tissue Activator D-44, Tissue Activator D 44, Tisokinase, Tissue-Type Plasminogen Activator, Tissue Type Plasminogen Activator, TTPA, T-Plasminogen Activator, T Plasminogen Activator, Alteplase, Activase, Actilyse, Lysatec rt-PA, Lysatec rt PA, Lysatec rtPA, , saruplase, prourokinase (enzyme-activating), recombinant unglycosylated single-chain urokinase-type plasminogen activator, pro-urokinase, Rescupase, A-74187, , Zocor, Darob, MJ-1999, MJ 1999, MJ1999, , telmisartan, Micardis, BIBR 277, BIBR-277, Pritor, , teneceplase, Metalyse, TNKase, Ticlopidine, Ticlopidine Hydrochloride, Ticlodix, Ticlodone, 53-32C, 53 32C, 5332C, Ticlid, , Timolol, Timoptic, Timoptol, Timolol Hemihydrate, Timacar, Timolol Maleate, MK-950, MK 950, MK950, Optimol, Blocadren, , tinzaparin, tinzaparin sodium, Innohep, tirofiban, tirofiban hydrochloride monohydrate, MK 383, MK-383, tirofiban hydrochloride, Aggrastat, Cahill May Roberts brand of tirofiban hydrochloride monohydrate, MSD brand of tirofiban hydrochloride monohydrate, Merck Frosst brand of tirofiban hydrochloride monohydrate, Merck Sharp and Dohme brand of tirofiban hydrochloride monohydrate, Agrastat, Merck brand of tirofiban hydrochloride monohydrate, L 700462, L-700462, , tolvaptan, OPC 41061, OPC-41061, Samsca, , topiramate, Topamax, Epitomax, McN 4853, McN-4853, , trandolapril, Odrik, Udrik, RU 44570, RU44570, RU-44570, Mavik, Gopten, triflusal, Disgren, Centrophne, Vastarel, Idaptan, Trimetazidine Irex, Vasartel, Trimetazidine Dihydrochloride, , Urokinase-Type Plasminogen Activator, Urokinase Type Plasminogen Activator, U-Plasminogen Activator, U Plasminogen Activator, U-PA, Urinary Plasminogen Activator, Urokinase, Renokinase, Abbokinase, Kidney Plasminogen Activator, Single-Chain Urokinase-Type Plasminogen Activator, Single Chain Urokinase Type Plasminogen Activator, , valsartan, Diovan, Tareg, KalpressMiten, Provas, Vals, valsartan, CGP 48933, Nisis, Aventis brand of valsartan, , Verapamil, Iproveratril, Cordilox, Dexverapamil, Falicard, Izoptin, Isoptine, Isoptin, Lekoptin, Verapamil Hydrochloride, Calan, Finoptin, , vesnarinone, OPC 8212, OPC-8212, , Xamoterol, Corwin, ICI-118587, ICI 118587, ICI118587, Xamoterol Fumarate, Xamoterol Hemifumarate, Xamoterol Monohydrobromide, Xamoterol Monohydrochloride, Xamtol, Carwin, Xamoterol Maleate (2:1), , ximelagatran, xi-melagatran, Exanta, H 376 95, H 376-95, , Glucotrol, Warfarin, Coumadine, Apo-Warfarin, Gen-Warfarin, Warfant, Coumadin, Marevan, Warfarin Potassium, Warfarin Sodium, Aldocumar, Tedicumar, , reviparin, reviparine, reviparin-sodium, reviparin sodium, LU 47311, LU-47311, Clivarin, Abbott brand of reviparin-sodium, Clivarine, ICN brand of reviparin-sodium, , Propafenone, Propamerck, Rythmol, Arythmol, Rytmonorm, Nor-

fenon, Pintoform, Propafenon Minden, Rytmo-Puren, Rytmogenat, Baxarytmon, Cuxafenon, Fenoprain, Jutanorm, Nistaken, Prolecofen, , nateglinide, nate-glinide, senaglinide, IPCCPA, AY 4166, AY-4166, DJN 608, Starsis, Starlix, Novartis brand of nateglinide, A 4166, A-4166, Fastic, , Bay K 5552, , Metformin, Dimethylguanylguanidine, Dimethylbiguanidine, Glucophage, , Glyburide, Glybenclamide, Glibenclamide, Diabeta, Euglucon 5, Neogluconin, HB-419, HB 419, HB419, HB-420, HB 420, HB420, Maninil, Micronase, Daonil, Euglucon N, , 4-transhydroxy glyburide, , Glucovance, Glyburide-metformin, , Integrilin, Integrelin, reteplase, Retavase, Rapilylsin, Betaxolol, SL-75212, SL 75212, SL75212, Betoptic, Betoptima, Betaxolol, Oxodal, ALO-1401-02, ALO 1401 02, ALO140102, Betaxolol, Lipitor, torcetrapib, CP 529414, CP529414, CP-529414, , CYPHER, , XIENCE V, Guidant XIENCE V, Abbott XIENCE V, XIENCE 5, Endeavour, Medtronic Endeavour, albiglutide, , liraglutide, victoza, exenatide, exendin 4, exendin-4, Ex4 peptide, Byetta, AC 2993, AC 2993 LAR, , sitagliptin, sitagliptin phosphate, Januvia, MK 0431, MK0431, MK-0431, , Acenocoumarol, Nicoumalone, Acenocoumarin, Synthrome, Synthrom, Syncoumar, Syncumar, Sinkumar, Sintrom, Mini-Sintrom, Mini Sintrom, MiniSintrom, , Tissue Plasminogen Activator, Tissue Activator D-44, Tissue Activator D 44, Tisokinase, Tissue-Type Plasminogen Activator, Tissue Type Plasminogen Activator, TTPA, T-Plasminogen Activator, T Plasminogen Activator, Alteplase, Activase, Actilyse, Lysatec rt-PA, Lysatec rt PA, Lysatec rtPA, , Bepidil Monohydrochloride, Vascor, Bedapin, CERM-1978, CERM 1978, CERM1978, 1978-CERM, 1978 CERM, 1978CERM, Cordium, Unicordium, Bepadin, , Ethyl Chlorophenoxyisobutyrate, Atromid, Atromid S, Miscleron, Miskleron, Athromidin, , elinogrel, PRT 060128, PRT060128, PRT-060128, , Brain Natriuretic Peptide, BNP-32, BNP 32, Nesiritide, B-Type Natriuretic Peptide, BNP Gene Product, Type-B Natriuretic Peptide, Type B Natriuretic Peptide, Natriuretic Peptide Type-B, Natriuretic Peptide Type B, Natriuretic Factor-32, Natriuretic Factor 32, Brain Natriuretic Peptide-32, Brain Natriuretic Peptide 32, Natrecor, , Phenindione, Phenylindanedione, Phenylene, Pindione, Fenilin, Dindevan, , repa-glinide, AG-EE 388 ZW, NovoNorm, GlucoNorm, Prandin, AG-EE 388, AG-EE 623 ZW, , Brilique, Brilinta, AZD 6140, AZD6140, AZD-6140, zofenopril, Zofenil, Zofil, SQ 26900, SQ-26900, SQ 26991, SQ-26991, , SQ 26703, zofenopril-SH, zofenopril-SH cpd with arginine, , MK 0859, MK0859, MK-0859, , PRT054021, , blufomedil, bufomedil, Buflor AbZ, AbZ brand of buflomedil hydrochloride, Buflor-POS, Ursapharm brand of buflomedil hydrochloride, Buflor-Puren, Alpharma brand of buflomedil hydrochloride, Buflorhexal, Hexal brand of buflomedil hydrochloride, Buflomedil Heumann, Heumann brand of buflomedil hydrochloride, buflomedil hydrochloride, Buflomedil Lindo, Lindopharm brand of buflomedil hydrochloride, buflomedil pyridoxal phosphate, Buflomedil Stada, Stadapharm brand of buflomedil hydrochloride, buflomedil von ct, ct-Arzneimittel brand of buflomedil hydrochloride, Buflomedil-ratiopharm, ratiopharm brand of buflomedil hydrochloride, Fonzylane, Lafon brand of buflomedil hydrochloride, LL 1656, Loftyl, Bufedil, Lofton, Abbott brand of buflomedil hydrochloride, Sinaxis, Hosbon brand of buflomedil hydrochloride, Buflor 1A Pharma, 1A brand of buflomedil hydrochloride, , Folic Acid, Vitamin M, Pteroylglutamic Acid, Folate, Folvite, Folacin, , Hydrochlorothiazide, HCTZ, Dichlothiazide, Dihydrochlorothiazide, HydroDIURIL, Oretic, Sectrazide, Esidrix, Esidrex, Hypothiazide, , inogatran, N-(2-(2-(((3-((aminoiminomethyl)amino)propyl)amino)carbonyl)-1-piperidinyl)-1-(cyclohexylmethyl)-2-oxo-ethyl)glycine, H 314-27, H314-27, H-314-27, , voglibose, Basen, , Trepidil, Trapymine, Rocornal, , desdiethyltrapidil, N-dediethyltrapidil, desdiethyl-trapidil, , certoparin, certoparin sodium, Mono-Embolex, Novartis brand of certoparin sodium, Alphaparin, Grifols brand of certoparin sodium, , glimepiride, glymepiride, HOE 490, HOE-490, Roname, Amaryl, Amarel, hydroxyglimepiride, hydroxy-glimepiride, , Linagliptin, Tradjenta, BI 1356, BI1356, BI-1356, , taspoglutide, , miti-glinide, KAD 1229, KAD-1229, , transcatheter aortic valve implantation, , sibutramine, Meridia, mono-desmethylsibutramine, BTS 54 524, BTS-54524, BTS 54524, Reductil, di-desmethylsibutramine, didesmethylsibutramine, (R)-DDMS, sibutramine hydrochloride, , saxagliptin, Onglyza, BMS 477118, BMS477118, BMS-477118, , eplerenon, Inspra, CGP 060536B, CGP060536B, CGP-060536B, Tekturna, SPP100, , SYR 322, SYR322, SYR-322, , benfluramate, benfluorex maleate, SE 780, 780 SE, JP 992, Mediator trade name of benfluorex hydrochloride, Biopharma brand of benfluorex hydrochloride, Modulator trade name of benfluorex hydrochloride, Servier brand of benfluorex hydrochloride, S 780, benfluorex hydrochloride, 1-(2-trifluoromethylphenyl)-2-(benzoyloxyethyl)aminopropane HCl, , Coronary Artery Bypass, Coronary Artery Bypasses, Coronary Artery Bypass Surgery, Aortocoronary Bypass, Aortocoronary Bypasses, Coronary Artery Bypass Grafting, CABG, AR C69931MX, AR-C69931MX, , Carotid Endarterectomy, Carotid Endarterectomies, , Chlortalidone, Phthalamudine, Chlorphthalidolone, Oxodoline, Thalitone, Hygroton, , dofetilide, 1-(4-methanesulfonamidophenoxy)-2-(N-(4-methanesulfonamidophenethyl)-N-methylamine)ethane, 1-MSPMPE, Tikosyn, UK 68798, , docetaxol, Taxoltere metro, Taxotere, NSC 628503, RP 56976, RP-56976, ebselen, PZ 51, PZ-51, RP 60931, DR 3305, DR-3305, , Fenoximone, Perfan, MDL 19438, MDL-17043, MDL 17043, MDL17043, , enoximone sulfoxide, MDL 17043 sulfoxide, , Exercise Therapy, Exercise Therapies, , Gene Therapy, DNA Therapy, Somatic Gene Therapy, , Ginkgo biloba, Ginkgo bilobas, Ginko, Ginkos, Ginkgo, Ginkgos, Gingko, Gingkos, Maidenhair Tree, Maidenhair Trees, Gingko biloba, Ginkgo bilobas, Ginkgophyta, Ginkgophytas, , Lacipil, Lacimen, Caldine, Motens, GR 43659X, GR-43659X, , olmesartan medoxomil, CS 866, CS-866,

Votum, Benicar, Olmetec, , h5G1.1-scFv, pexelizumab, , Dalteparin, Tedelparin, Kabi-2165, Kabi 2165, Kabi2165, Fragmin, Fragmine, Dalteparin Sodium, FR-860, FR 860, FR860, , efegatran, Me-Phe-Pro-Arg-H, D-methyl-phenylalanyl-prolyl-arginal, GYKI 14766, GYKI-14766, LY 294468, LY-294468, efegatran sulfate, , etofibrate, Lipo-Merz, Merz brand of etofibrate, Tricerol, Armstrong brand of etofibrate, etofibrate hydrochloride, , simendan, OR-1855, Simadax, dextrosimendan, OR 1259, OR-1259, , ZP10A peptide, AVE 0010, AVE0010, AVE-0010, Lixisenatide, AQVE-10010, , primary ballon angioplasty, primary PTCA, vildagliptin, (2S)-(((3-hydroxyadamantan-1-yl)amino)acetyl)pyrrolidine-2-carbonitrile, NVP-LAF237, Galvus, , Gliclazide, Glyclazide, Gliklazid, Diamcron, S-1702, S 1702, S1702, S-852, S 852, S852, Diaglyk, Gen-Gliclazide, Gen Gliclazide, Glyade, Novo-Gliclazide, Novo Gliclazide, Diaikron, Diabrezide, , Qnexa, Zontivity, SCH 530348, SCH530348, SCH-530348, , MDX-1106, ONO-4538, BMS-936558, Opdivo, lambrolizumab, Keytruda, MK-3475, , MDX-CTLA-4, Yervoy, DX 010, MDX010, MDX-010, , Iressa, ZD1839, ZD 1839, , Anzatax, NSC-125973, NSC 125973, NSC125973, Taxol, Taxol A, Bris Taxol, Paxene, Praxel, 7-epi-Taxol, 7 epi Taxol, Onxol, SDZ RAD, SDZ-RAD, 40-O-(2-hydroxyethyl)-rapamycin, RAD 001, RAD001, Afinitor, Certican, , pertuzumab, Perjeta, Omnitarg, ado-trastuzumab emtansine, trastuzumab-DM1, trastuzumab-DM1 conjugate, T-DM1 cpd, trastuzumab emtansine, huN901-DM1, Kadcyca, Avastin, , gemcitabine, dFdCyd, 2'-deoxy-2'-difluorocytidine, gemcitabine hydrochloride, LY 188011, LY-188011, Gemzar, , Toremifene, Toremifene Citrate, Toremifene Citrate (1:1), Fareston, FC-1157a, FC 1157a, FC1157a, , Xeloda, , Cisplatin, cis-Diamminedichloroplatinum(II), Platinum Diamminodichloride, cis-Platinum, cis Platinum, Dichlorodiammineplatinum, cis-Diamminedichloroplatinum, cis Diamminedichloroplatinum, cis-Dichlorodiammineplatinum(II), NSC-119875, Platino, Platinol, Biocisplatinum, Platidium, , ICI 182780, ICI-182780, ZM 182780, ZM-182780, Faslodex, , palbociclib, Ibrance, PD 0332991, PD0332991, PD-0332991, anastrozole, anastrazole, ICI D1033, ZD-1033, Zeneca ZD 1033, ZD1033, Arimidex, letrozole, Femara, Fmara, CGS 20267, CGS-20267, Aminoglutethimide, Cytadren, Orimeten, formestane, 4-hydroxyandrostenedione, 4-OHA, Lentaron, CGP-32349, CGP 32 349, CGP 32349, , exemestane, FCE 24304, FCE-24304, Aromasil, Aromasin, Aromasine, , Fadrozole, CGS-16949A, CGS 16949A, CGS16949A, Fadrozole Hydrochloride, Fadrozole Monohydrochloride, CGS 020286A, CGS020286A, CGS-020286A, FAD 286, FAD286, FAD-286, , Tamoxifen, ICI-47699, ICI 47699, ICI47699, Nolvadex, Novaldex, Tamoxifen Citrate, Tomaxithen, Zitazonium, ICI-46474, ICI 46474, ICI46474, Soltamox, ixabepilone, BMS247550, BMS-247550, BMS 247550, Herceptin, Torisel, CCI 779, CCI-779, , alirocumab, REGN727 monoclonal antibody, monoclonal antibody REGN727, SAR236553, Praluent, , AMG 145, evolocumab, AMG-145, Repatha, Medroxyprogesterone Acetate, Medroxyprogesterone 17-Acetate, Medroxyprogesterone 17 Acetate, Depo-Medroxyprogesterone Acetate, Depo Medroxyprogesterone Acetate, 6-alpha-Methyl-17alpha-hydroxyprogesterone Acetate, 6 alpha Methyl 17alpha hydroxyprogesterone Acetate, Curretab, Cycrin, Depo-Provera, Depo Provera, DepoProvera, Farlutal, Perlutex, Provera, Veramix, Clinovir, Gestapuran, sorafenib, sorafenib N-oxide, 4-(4-(3-(4-chloro-3-trifluoromethylphenyl)ureido)phenoxy)pyridine-2-carboxylic acid methamide-4-methylbenzenesulfonate, BAY 545-9085, BAY-545-9085, sorafenib tosylate, BAY 43-9006, Nexavar, , entinostat, SNDX-275, MS 27-275, MS-275, MS 275, MS-27-275, B 1939, B-1939, E 7389, E-7389, Halaven, NSC 707389, NSC707389, NSC-707389, B 1793, B-1793, ER-086526, ER086526, ER 086526, ER-86526, , Abraxane, vinorelbine, 5'-nor-anhydrovinblastine, Navelbine, vinorelbine tartrate, KW 2307, KW-2307, , intensive treatment, tighter control of blood pressure, low target blood pressure, strict blood pressure control, intensified blood-pressure control, IMC C225, IMC-C225, MAb C225, C225, Erbitux, , Tarceva, CP 358774, CP-358774, OSI-774, Inlyta, AG 013736, AG013736, AG-013736, , TKI 258, TKI258, TKI-258, dovitinib, CHIR 258, CHIR258, CHIR-258, , GW 786034B, GW786034B, GW-786034B, GW 780604, GW780604, GW-780604, Votrient, , Sutent, SU 11248, SU11248, SU-11248, SU011248, SU 011248, SU-011248, , D2E7 Antibody, Humira, Cimzia, Cimzias, CDP870, CDP870s, CDP 870, CDP 870s, , TNF Receptor Type II-IgG Fusion Protein, TNF Receptor Type II IgG Fusion Protein, Enbrel, Recombinant Human Dimeric TNF Receptor Type II-IgG Fusion Protein, Recombinant Human Dimeric TNF Receptor Type II IgG Fusion Protein, TNFR-Fc Fusion Protein, TNFR Fc Fusion Protein, TNR-001, TNR001, TNR 001, TNT Receptor Fusion Protein, TNTR-Fc, , Simponi, , MAb cA2, Monoclonal Antibody cA2, Remicade, , Interleukin 1 Receptor Antagonist Protein, Urine-Derived IL1 Inhibitor, Urine Derived IL1 Inhibitor, IL1 Febrile Inhibitor, Urine IL-1 Inhibitor, IL-1Ra, Antril, Kineret, Anakinra, , tocilizumab, atlizumab, Actemra, , Rituxan, MabThera, Zytux, Rituximab, Rituximab CD20 Antibody, Mabthera, IDEC-C2B8 Antibody, IDEC C2B8 Antibody, IDECC2B8 Antibody, IDEC-C2B8, IDEC C2B8, IDECC2B8, GP2013, Rituxan, , tasocitinib, tofacitinib citrate, Xeljanz, CP690550, CP-690550, CP 690550, , durvalumab, Imfinzi, MPDL3280A, Tecentriq, RG7446, RG-7446, , MTA, Pemetrexed Disodium, LY 231514, LY231514, LY-231514, Alimta, , rolofylline, KW 3902, KW-3902, MK 7418, MK7418, MK-7418, , BG 9928, BG-9928, BG9928, BIO 4683, BIO4683, BIO-4683, BIO 5770, BIO5770, BIO-5770, BIO 8170, BIO8170, BIO-8170, BIO 9002, BIO9002, BIO-9002, tonapofylline, BIO 7505, BIO7505, BIO-7505, , Invokana, , BI 10773, BI10773, BI-10773, Jardiance, , dapagliflozin, forxiga, BMS 512148, BMS512148, BMS-512148, , avelumab, MSB0010718C, , Xalkori, PF-02341066, PF02341066, PF 02341066, , BAY 94-8862, finerenone, , AZD 2281, AZD2281, AZD-

2281, AZD221, Lynparza, , 2-(4-(piperidin-3-yl)phenyl)-2H-indazole-7-carboxamide, niraparib hydrochloride, MK 4827, MK4827, MK-4827, , BMN 673, , 2-((R)-2-methylpyrrolidin-2-yl)-1H-benzimidazole-4-carboxamide, 2-(2-methylpyrrolidin-2-yl)-1H-benzimidazole-4-carboxamide, ABT 888, ABT888, ABT-888, , bococizumab, , CH5424802, alectinib, RO5424802, , ceritinib, Zykadia, LDK378, , AP26113, brigatinib, , caprelsa, ZD 6474, ZD6474, ZD-6474, vandetanib, Zactima, , imetelstat, motesanib, motesanib diphosphate, AMG 706, AMG706, AMG-706, , aflibercept, VEGF Trap-Eye, VEGF Trap - regeneron, VEGF-Trap, AVE 005, AVE005, AVE-005, Zaltrap, ZIV-aflibercept, AVE 0005, AVE0005, AVE-0005, eylea, , osimertinib, Tagrisso, , rucaparib, AG 014699, AG014699, AG-014699, PF-01367338, , cabozantinib, Cometriq, XL 184, XL184 cpd, XL-184, BMS 907351, BMS907351, BMS-907351, , abemaciclib, LY2835210, LY2385219, Verzenio, ribociclib, LEE011, , vemurafenib, Zelboraf, R05185426, RG7204, RG-7204, PLX4032, PLX 4032, , ticilimumab, CP 675, P675 cpd, CP-675, CP-675,206, CP-675206, CP675206, CP 675206,

## 8 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.