Clinical trials of anti hypertensive agent for diabetes type 2 in patients with or without hypertension

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1 ACE inhibitor

Trial	Treatments	Patients	Trials design and methods
captopril or atenolol vs control			
UKPDS 38 , 1998 n=758/390 follow-up: 8.4y (median)	tight control of blood pressure aiming at a BP <150/85 (with the use of captopril or atenolol as main treatment, other treatment were added if the control criteria were not met) versus less tight control aiming at a blood pressure of <180/105 (avoiding treatment with ACE inhibitors or beta-blockers)	hypertensive patients with type 2 diabetes	Parallel groups open UK
ACE inhibitor vs placebo			
HOPE (diabetic subgroup) , 2000 n=1808/1759 follow-up: 4.5 years	ramipril 10 mg once per day orally versus placebo	patients with diabetes (sub group), aged 55 years or older, who had a previous cardiovascular event or at least one other cardiovascular risk factor, no clinical proteinuria, heart failure, or low ejection fraction	Factorial plan double-blind North, South america, Europe
enalapril vs placebo			
SCAT (diabetic subgroup) , 2000 n=25/25 follow-up: Jun 1991 - Jul 1995	enalapril 2.5mg twice daily versus placebo	normocholesterolemic patients	Factorial plan double-blind Canada
SOLVD (subgroup) , 1996 n=646/664 follow-up: 3.5y	enalapril versus placebo	patients with chronic heart failure	Parallel groups double-blind
perindopril vs placebo			
EUROPA (PERSUADE substudy) , 2005 n=721/781 follow-up: 4.3y	perindopril 8mg once daily versus placebo	patients with known coronary artery disease and without heart failure, sub group of diabetic patients	Parallel groups double-blind
PROGRESS (diabetic subgroup) , 2001 n=393/368 follow-up: 3.9 y	perindopril 4 mg daily versus placebo	hypertensive and non-hypertensive individuals with cerebrovascular disease, subgroup of diatebic patients	Parallel groups double-blind
perindopril and indapamide vs placebo			

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Trial	Treatments	Patients	Trials design and methods
ADVANCE , 2007 [NCT00145925] n=NA follow-up:	fixed combination of perindopril and indapamide versus placebo	patients with type 2 diabetes irrespective of initial blood pressure levels or the use of other blood pressure lowering drugs	
ADVANCE , 2007 [NCT00145925] n=5569/5571 follow-up: 4.3 yrs	low-dose fixed combination of perindopril and indapamide versus placebo	individuals with type 2 diabetes	Factorial plan double-blind Asia, Australasia, Europe, and North America
ramipril vs placebo			
DIABHYCAR , 2004 n=2443/2469 follow-up: median 4 years	ramipril 1.25 mg/day versus placebo	patients with type 2 diabetes who have microalbuminuria or proteinuria	Parallel groups double-blind Europe, North Africa
DREAM , 2008 n=2623/2646 follow-up: 3 years	ramipril(up to 15 mg per day) versus placebo	people aged >=30 years, with Impaired glucose tolerance and/or impaired fasting glucose without known CVD or renal insufficiency	Factorial plan open
captopril vs atenolol			
UKPDS 39 , 1998 n=400/358 follow-up: ND	captopril 25 mg/d aiming at a BP <150/85 versus atenolol 50mg/d aiming at a BP <150/85	hypertensive patients with type 2 diabetes	Parallel groups open UK
ACE inhibitor vs CCB			
STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000 n=235/231 follow-up: 5.03y	ACE inhibitor versus calcium antagonists	diabetic (subgroup) elderly patients aged 70-84 years	open with blind assessment Sweden
lisinopril vs chlorthalidone			
ALLHAT (lisi vs chlor, diabetic subgroup) , 2002 n=2431/4498 follow-up: 4.9 y	lisinopril 10 to 40 mg/d versus chlorthalidone 12.5 to 25 mg/d	diabetic (subgroup) participants aged 55 years or older with hypertension	Parallel groups double-blind
captopril vs diuretic and/or beta-blockers			
CAPP (diabetic subgroup) , 1999 n=309/263 follow-up: 6.1 year	Captopril initial dose of 50 mg daily given in one or two doses versus thiazide diuretic or beta-blocker	Patients aged 25-66 years with a measured diastolic blood pressure of 100 mm Hg or more on two occasions; subgroup of diabetic patients	Parallel groups open with blinded assessment Sweden, Finland
ACE inhibitor vs diuretic or beta-blocker			
STOP-2 ACEI (diabetic subgroup) , 2000 n=235/253 follow-up: 5.03y	ACE inhibitor versus conventional treatment (diuretic or beta-blocker)	diabetic (subgroup) elderly patients aged 70-84 years with hypertension	Parallel groups open with blind assessment Sweden

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2 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
candesartan vs control			
SCOPE (diabetic subgroup) , 2003 n=313/284 follow-up: 3.7 years	candesartan versus control	sub group of diabetic patients aged 70-89 years, with systolic blood pressure 160-179 mmHg, and/or diastolic blood pressure 90-99 mmHg, and a Mini Mental State Examination (MMSE) test score >or= 24	Parallel groups double-blind 15 countries
irbesartan vs placebo			
IDNT irbesartan , 2001 n=579/569 follow-up: 2.6 years	Irbesartan 300 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double blind Worldwide
IPDM 150mg , 2001 n=195/201 follow-up: 2 years	irbesartan 150 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind Worldwide
losartan vs placebo			
RENAAL , 2001 n=751/762 follow-up: 3.4 y	losartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind America, Europe, Asia
olmesartan vs placebo			
ROADMAP , 2010 [NCT00185159] n=2232/2215 follow-up: 3.2 y	olmesartan at 40 mg/day versus placebo	patients with diabetes and at least one additional cardiovascular risk factor, but no evidence of renal dysfunction	Parallel groups double-blind Europe (19 countries)
ORIENT [NCT00141453] n=282/284 follow-up:	olmesartan versus placebo	patients with diabetic Nephropathy and overt proteinuria secondary to type 2 diabetes mellitus	Parallel groups double-blind Japan, Hong Kong
telmisartan vs placebo			
PROFESS , 2008 n=2840/2903 follow-up: 2.4y	80 mg telmisartan once daily versus placebo	-	Parallel groups double-blind
irbesartan vs amlodipine			

continued...

Trial	Treatments	Patients	Trials design and methods
IDNT (irbesartan vs amlodipine) , 2001 n=579/567 follow-up: 2.6 years	Irbesartan 300 mg daily versus amlodipine 10 mg daily	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double blind Worldwide
valsartan vs amlodipine			
NAGOYA HEART , 2011 *unpublished* [NCT00129233] n=575/575 follow-up: 3.2 y median	blood-pressure-lowering therapy based on valsartan; blood-pressure goal of <130/80 mm Hg versus blood-pressure-lowering therapy based on amlodipine; blood-pressure goal of <130/80 mm Hg	patients with hypertension with type 2 diabetes or impaired glucose tolerance	Parallel groups open Japan
losartan vs atenolol			
LIFE (diabetic subgroup) , 2002 n=586/609 follow-up: 4.7 years	losartan 50mg daily at step 1 versus atenolol 50mg daily at step 1	patients with diabetes (subgroup) , hypertension, and signs of left-ventricular hypertrophy on electrocardiograms	Parallel groups double-blind USA, UK, Nordic countries
temisartan vs enalapril			
DETAIL , 2004 n=120/130 follow-up: 5 years	telmisartan 80 mg daily versus enalapril 20 mg daily	subjects with type 2 diabetes and early nephropathy	Parallel groups double-blind northern Europe

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3 Angiotensin-Converting Enzyme Inhibitors

Trial	Treatments	Patients	Trials design and methods
perindopril and indapamide vs placebo			
ADVANCE , 2007 [NCT00145925] n=NA follow-up:	fixed combination of perindopril and indapamide versus placebo	patients with type 2 diabetes irrespective of initial blood pressure levels or the use of other blood pressure lowering drugs	
ADVANCE , 2007 [NCT00145925] n=5569/5571 follow-up: 4.3 yrs	low-dose fixed combination of perindopril and indapamide versus placebo	individuals with type 2 diabetes	Factorial plan double-blind Asia, Australasia, Europe, and North America

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4 beta-blockers

Trial	Treatments	Patients	Trials design and methods
metoprolol vs placebo			
MERIT-HF , 2005 n=495/490 follow-up: 1y	metoprolol CR/XL versus placebo	patients with CHF NYHA classe 2 to 4 and EF<=40% sub group of diabetic patients	Parallel groups double-blind USA and Europe
carvedilol vs metoprolol			
GEMINI , 2004 n=498/737 follow-up: 5 months	6.25- to 25-mg dose of carvedilol twice daily versus 50- to 200-mg dose of metoprolol tartrate twice daily	patients with hypertension and type 2 diabetes mellitus receiving renin-angiotensin system blockade	Parallel groups double-blind

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5 calcium blockers

Trial	Treatments	Patients	Trials design and methods
verapamil vs control			
INVEST (subgroup) , 2003 n=3169/3231 follow-up: 24 months	calcium antagonist strategy (verapamil sustained release) versus non-calcium antagonist strategy (atenolol)	hypertensive CAD patients aged 50 years or older	Parallel groups open 14 countries
amlodipine vs placebo			
IDNT amlodipine , 2001 n=567/569 follow-up: 2.6 years	Amlodipine 10 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind Worldwide
nifedipine vs placebo			
ACTION , 1998 n=565/545 follow-up: 4.9y	Nifedipine GITS versus placebo	patients aged at least 35 years with stable angina pectoris and proven coronary artery disease; subgroup of diabetic patients	Parallel groups double-blind 19 countries
nitrendipine vs placebo			
Syst-Eur (diabetic subgroup) , 1999 n=252/240 follow-up: 2 years	Calcium-channel blocker versus placebo	subgroup of diabetic patients, age, >=60 years) with systolic blood pressure of 160 to 219 mm Hg and diastolic pressure below 95 mm Hg	Parallel groups double blind
nifedipine vs ACE inhibitor			
JMIC-B (diabetic subgroup) , 2004 n=199/173 follow-up: 3 years	nifedipine retard versus angiotensin converting enzyme inhibitors	outpatients aged under 75 years who had diagnoses of both hypertension and coronary artery disease	Parallel groups open Japan
amlodipine vs atenolol			
ASCOT (subgroup) , 2008 n=2565/2572 follow-up: 5.7y	amlodipine with addition of perindopril as required versus atenolol with addition of thiazide as required	Patients with untreated hypertension or treated hypertension; diabetic subgroup with two additionnal risk factors	Parallel groups double-blind
benazepril + amlodipine vs benazepril + hydrochlorothiazide			
ACCOMPLISH (diabetic subgroup) , 2010 [NCT00170950] n=1432/1410 follow-up: 36 months	benazepril, combined with amlodipine versus benazepril, combined with hydrochlorothiazide	patients with diabetes (subgroup) and hypertension at high risk of cardiovascular and related events	Parallel groups double-blind US, Norway, Denmark, Finland
amlodipine vs chlorthalidone			
ALLHAT (amlodipine vs chlor, diabetic subgroup) , 2002 n=2664/4498 follow-up: 4.9 y	amlodipine versus chlorthalidone	diabetic (subgroup) participants aged 55 years or older with hypertension	Parallel groups double-blind
nifedipine vs coamilozide			

continued...

Trial	Treatments	Patients	Trials design and methods
INSIGHT (diabetic subgroup) , 2000 n=649/653 follow-up: 4 y	Nifedipine GITS 30 mg daily versus co-amilozide hydrochlorothiazide 25 mg plus amiloride 2.5 mg	diabetic (subgroup) patients aged 55-80 years with hypertension (blood pressure >= 150/95 mm Hg, or >= 160 mmHg systolic)	Parallel groups double-blind Europe, Israel
calcium-channel blocker vs diuretic or beta-blocker			
STOP-2 CCB (diabetic subgroup) , 2000 n=231/253 follow-up: 5.03y	Calcium-channel blocker versus diuretic or beta-blocker	diabetic (subgroup) elderly patients aged 70-84 years	Parallel groups open with blind assessment Sweden
diltiazem vs diuretic or beta-blocker			
NORDIL (diabetic subgroup) , 2000 n=351/376 follow-up: 4.5 y	Diltiazem 180360 mg diltiazem daily at step one versus thiazide diuretic or a beta-blocker at step one	diabetic patients (subgroup), aged 50-74 years who had diastolic blood pressure of 100 mm Hg or more	Parallel groups open Norway, Sweden
nisoldipine vs enalapril			
ABCD hypertension , 1998 n=235/235 follow-up: 5 y	nisoldipine (long acting) versus enalapril	patients with non-insulin-dependent diabetes and hypertension	Factorial plan Double blind USA
amlodipine vs fosinopril			
FACET , 1997 n=191/189 follow-up: 3.5 y	amlodipine (long acting) 10 mg daily versus fosinopril 20 mg daily	hypertensive patients with NIDDM	Parallel groups open Italy

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6 diuretics

Trial	Treatments	Patients	Trials design and methods
chlorthalidone vs placebo			
SHEP (diabetic subgroup) , 1996 n=283/300 follow-up: 5 year	low dose of chlorthalidone (12.5-25.0 mg/d) with a step-up to atenolol (25.0-50.0 mg/d) or reserpine (0.05-0.10 mg/d) if needed versus placebo	men and women aged 60 years and older , non-insulin-treated diabetic (sub group) patients with isolated systolic hypertension (systolic BP >= 160 mm Hg; diastolic BP, <90 mm Hg)	Parallel groups double-blind

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7 intensive treatment

Trial	Treatments	Patients	Trials design and methods
intensive vs usual			
ABCD normotensives , 1993 n=237/243 follow-up: 5.3 y	intensive (10 mm Hg below the baseline DBP) DBP control versus moderate (80 to 89 mm Hg) DBP control	normotensive type 2 diabetic patients	Parallel groups open
ACCORD blood pressure , 2010 [NCT00000620] n=2363/2371 follow-up: 4.7 y	intensive blood-pressure control, targeting a systolic pressure of less than 120 mm Hg versus standard blood-pressure control	high-risk patients with type 2 diabetes, high HbA1c concentrations (>7.5%), and cardiovascular disease (or >=2 cardiovascular risk factors)	Factorial plan open United States, Canada
HOT <=80 (diabetic subgroup) , 1998 n=499 follow-up: 3.8y	target diastolic blood pressure <=80 mmHg versus target diastolic blood pressure <=90 mmHg	patients aged 50-80 years with hypertension and diastolic blood pressure between 100 mm Hg and 115 mm Hg; diabetics subgroup	Parallel groups open 26 countries

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8 About TrialResults-center.org

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