Clinical trials of anti hypertensive agents for diabetes type 2 in patients with hypertension

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1 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
irbesartan vs placebo			
IDNT (irbesartan vs pbo) , 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
irbesartan vs amlodipine			
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NAGOYA HEART , 2011 *unpublished* [NCT00129233] n=575/575 follow-up: 3.2 y median	blood-pressure-lowering therapy based on valsartan; blood-pressure goal of 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

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IPDM (150mg), 2001:

Parving HH, Lehnert H, Brchner-Mortensen J, Gomis R, Andersen S, Arner P The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes.

N Engl J Med 2001;345:870-8 [11565519]

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NAGOYA HEART, 2011:

Matsushita K, Muramatsu T, Kondo T, Maeda K, Shintani S, Murohara T Rationale and design of the NAGOYA HEART Study: comparison between valsartan and amlodipine regarding morbidity and mortality in patients with hypertension and glucose intolerance. J Cardiol 2010;56:111-7 [20409690] 10.1016/j.jjcc.2010.03.004

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2 angiotensin-converting enzyme inhibitors

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 inhibitors 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
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 calcium-channel blocker			

continued...

Trial	Treatments	Patients	Trials design and methods
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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STOP-2 (ACEI vs CCB) (diabetic subgroup), 2000:

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ALLHAT (lisi vs chlor, diabetic subgroup), 2002:

Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981-97 [12479763]

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3 calcium-channel blockers

Trial	Treatments	Patients	Trials design and methods
amlodipine vs placebo			
IDNT (amlodipine vs PBO) , 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
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
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			

continued...

Trial	Treatments	Patients	Trials design and methods
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			
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
diltiazem vs diuretic and/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
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
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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Brown MJ, Palmer CR, Castaigne A, de Leeuw PW, Mancia G, Rosenthal T, Ruilope LM Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT). Lancet 2000;356:366-72 [10972368] 10.1016/S0140-6736(00)02527-7

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ABCD (hypertension), 1998:

Estacio RO, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schrier RW The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. N Engl J Med 1998;338:645-52 [9486993] 10.1056/NEJM199803053381003

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4 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

References

SHEP (diabetic subgroup), 1996:

Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, Camel G, Davis BR, Frost PH, Gonzalez N, Guthrie G, Oberman A, Rutan GH, Stamler J Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. JAMA 1996;276:1886-92 [8968014]

5 intensive treatment

Trial	Treatments	Patients	Trials design and methods
intensive vs usual			
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

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ACCORD (blood pressure), 2010:

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6 Treatment blood pressure target

Trial	Treatments	Patients	Trials design and methods
more intensive blood pressure lowering strategie vs less intensive blood pressure lowering strategie			
ABCD target (H) , 2000 n=237/233 follow-up: 5 year	intensive treatment with a diastolic blood pressure goal of 75 mmHg versus moderate treatment with a diastolic blood pressure goal of 80-89 mmHg	diabetes patients with DBP >=90 mmHg	Parallel groups open
ABCD target (N) , 2002 n=237/243 follow-up:	intensive treatment (diastolic blood pressure decrease of 10 mmHg below baseline DBP) versus moderate treatment (diastolic blood pressure goal of 80-89 mmHg)	diabetes patients with diastolic blood pressure between 80 and 89mmHg	Parallel groups open

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Estacio RO, Jeffers BW, Gifford N, Schrier RW Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and type 2 diabetes. Diabetes Care 2000;23 Suppl 2:B54-64 [10860192]

ABCD target (N) , 2002:

Schrier RW, Estacio RO, Esler A, Mehler P Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney Int 2002;61:1086-97 [11849464] 10.1046/j.1523-1755.2002.00213.x

7 About TrialResults-center.org

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