Clinical trials of antiplatelets drug for cardiovascular prevention in secondary prevention in patients with intermittent claudication

TrialResults-center www.trialresultscenter.org

1 clopidogrel

Trial	Treatments	Patients	Trials design and methods
clopidogrel vs aspirin			
CAPRIE , 1996 n=9599/9586 follow-up: mean 1.91 years	clopidogrel 75 mg once daily versus aspirin 325 mg once daily	patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	Parallel groups Double blind 16 countries
CAPRIE , 1996 n=3223/3229 follow-up: 1.91 y	Clopidogrel 75 mg versus Aspirine 325 mg	patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	Parallel groups double blind

References

CAPRIE, 1996:

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39 [8918275]

CAPRIE, 1996:

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39 [8918275]

2 platelet aggregation inhibitors

Trial	Treatments	Patients	Trials design and methods
vs			
Brittenden J *ongoing* n=NA follow-up:	-	-	
Brittenden J (2) *ongoing* n=NA follow-up:	-	100 patients (age 18-80 ans) avec claudication intermittente et ayant une lesion accessible l'angioplastie au niveau iliaque ou fmoral superficiel (chographie-doppler).	
Fowkes FGR *ongoing* n=NA follow-up:	aspirine absorption entrique 100 mg / j pendant 5 ans versus placebo	3300 patients suivis 5 ans avec atherosclrose asymptomatique, diagnostique par un ABI diminu.	

continued...

Trial	Treatments	Patients	Trials design and methods
McCollum CN *ongoing* n=NA follow-up:	-	48 patients avec AOMI	
ticagrelor vs clopidogrel			
EUCLID , 2016 [NCT01732822] n=NA	-	-	
vs placebo			
Hess (2) , 1985 n=80/80 follow-up:	Aspirine Dipyridamole 330 mg / j 225 mg / j versus Placebo	patients with occlusive arterial disease in the lower extremities	Parallel groups double blind
Schoop (2) , 1983 n=100/100 follow-up:	Aspirine Dipyridamole 990 mg / j 225 mg /j versus Placebo	AOMI stade non prcis	Parallel groups double blind
VA study , 1986 n=110/121 follow-up: 46 months	Aspirine + Dipyridamole 975 mg / j 225 mg /j versus Placebo	non-insulin-dependent diabetic men with either a recent amputation for gangrene or active gangrene	Parallel groups double blind
aspirin vs placebo			
CLIPS , 2007 n=185/181 follow-up: 20.7 months mean	oral aspirin 100 mg daily versus placebo	outpatients with stage I-II PAD documented by angiography or ultrasound, with ankle/brachial index <0.85 or toe index <0.6	Factorial plan double blind Europe
Munich B , 1975 n=42/40 follow-up:	Aspirine 1500 mg / jour pendant 24 mois versus Placebo	NA	Parallel groups double blind
Munich A , 1975 n=92/84 follow-up:	Aspirine: 1500 mg / jour versus Placebo	Donnes non disponibles	Parallel groups double blind
Schoop , 1983 n=100/100 follow-up: <5 y	groupe 1 : Aspirine 990 mg / j (pour mmoire : groupe 2 : Aspirine 990 mg / j + dipyridamole 225 mg/j) versus Placebo	AOMI stade non prcis	Parallel groups double blind
Hess , 1985 n=80/80 follow-up:	groupe 1 : Aspirine 330 mg / j (pour mmoire : groupe 2 : Aspirine 330 mg / j + dipyridamole 75 mg / j) versus Placebo	AOMI stade non prcis	Parallel groups single blind
cloricromene vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
CRAMPS , 2000 n=81/78 follow-up: 6 months	Cloricromne : 100 mg, 2 fois / jour / voie orale + aspirine : 160 mg / jour pendant 6 mois . versus placebo + aspirine: 160 mg/ jour pendant 6 mois.	Stade de la maladie : II, pendant 3.1 annes d'anciennet en moyenne dans les 2 groupes	Parallel groups double blind
ketanserine vs placebo			
Thulesius , 1987 n=79/86 follow-up: 6 months	Ketanserin 60 mg / j pdt 2 semaines 120 mg / j ensuite versus Placebo	patients with intermittent claudication (stade II)	Parallel groups double blind
Walden , 1991 n=17/18 follow-up: 15 months	Ketanserin 60 mg / j pdt 1 mois 120 mg / j ensuite versus Placebo	patients with intermittent claudication (stade II)	Parallel groups double blind
PACK , 1996 n=1930/1969 follow-up: 1 y	Ketanserin 40 mg / j pdt 1 mois 80 mg / j ensuite versus Placebo	patients over 40 years old who had had documented intermittent claudication for at least two months and in whom the ratio of systolic blood pressure in the ankle to that in the arm was less than or equal to 0.85 in both arteries of at least one foot	Parallel groups double blind
picotamide vs placebo			
Coto , 1989 n=20/20 follow-up: 6 months	Picotamide 900 mg / j versus Placebo	patients with peripheral occlusive arterial disease of the lower limbs at functional stage II of the Fontaine classification	Parallel groups double blind
ADEP , 1993 n=1150/1154 follow-up: 18 months	Picotamide 600 mg / j versus Placebo	patients with peripheral obstructive arterial disease (stade II+)	Parallel groups double blind
Neirotti , 1994 n=10/10 follow-up: 18 months	Picotamide 900 mg / j versus Placebo	patients with peripheral arterial disease (PAD) at functional stage 2 of the Fontaine classification and with intermittent claudication for at least six months	Parallel groups double blind
suloctidil vs placebo			
Adriaensen , 1976 n=15/15 follow-up: 2 months	Suloctidil 200 mg / j versus Placebo	patients suffering from intermittent claudication (stade II)	Parallel groups double blind
Verhaeghe , 1981 n=NA follow-up: 6 months	Suloctidil 200 mg / j versus Placebo	patients with intermittent claudication (stade II)	Parallel groups double blind
Jones , 1982 n=18/22 follow-up: 6 months	Suloctidil 300 mg / j versus Placebo	patients suffering from intermittent claudication (stade II)	Parallel groups double blind
Holm , 1984 n=20/20 follow-up: 2.75 y	Suloctidil 300 mg / j versus Placebo	AOMI stade II	Parallel groups double blind

continued...

Trial	Treatments	Patients	Trials design and methods
ticlopidine vs placebo			
Ellis , 1986 n=100/103 follow-up: 6 months	Ticlopidine 500 mg/j versus Placebo	AOMI stade II	Parallel groups double blind
Hurlow , 1980 n=30/30 follow-up:	Ticlopidine : 100 -500 mg / jour pendant 2 mois. versus Placebo	Donnes non disponibles	Parallel groups double blind
Krause , 1980 n=19/19 follow-up:	Ticlopidine : 500 mg pendant 4 mois versus Placebo	Donnes non disponibles	Parallel groups double blind
Katsumara , 1982 n=93/100 follow-up: 6 semaines	Ticlopidine 500 mg/j versus Placebo	patients with ischemic ulcers due to chronic arterial occlusion	Parallel groups double blind
Aukland , 1982 n=33/32 follow-up: 1 y	Ticlopidine 500 mg/j versus Placebo	men with atherosclerotic intermittent claudication and haemorheological abnormalities	Parallel groups double blind
Stiegler , 1984 n=57/57 follow-up:	Ticlopidine 500 mg/j versus Placebo	AOMI stade II	Parallel groups double blind
Cloarec , 1986 n=66/66 follow-up: 1 y	Ticlopidine 500 mg/j versus Placebo	AOMI stade non prcis	Parallel groups double blind
Arcan , 1988 n=83/86 follow-up: 6 months	Ticlopidine 500 mg/j versus Placebo	patients with chronic intermittent claudication due to obstructive peripheral vascular disease (stade II)	Parallel groups double blind
Balsano , 1989 n=76/75 follow-up: 21 months	Ticlopidine 500 mg/j versus Placebo	patients with intermittent claudication (stade II)	Parallel groups double blind
STIMS , 1990 n=346/341 follow-up: 5.6 y	Ticlopidine 500 mg/j versus Placebo	patients with intermittent claudication (stade II)	Parallel groups double blind
EMATAP , 1993 n=304/311 follow-up:	Ticlopidine 500 mg/j versus Placebo	AOMI stade non prcis	Parallel groups double blind
clopidogrel vs aspirin			
CAPRIE , 1996 n=9599/9586 follow-up: mean 1.91 years	clopidogrel 75 mg once daily versus aspirin 325 mg once daily	patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	Parallel groups Double blind 16 countries
CAPRIE , 1996 n=3223/3229 follow-up: 1.91 y	Clopidogrel 75 mg versus Aspirine 325 mg	patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	Parallel groups double blind

References

Brittenden J, 0:

A comparison of platelet activation in patients with intermittent claudication and healthy controls

Brittenden J (2), 0:

Randomised double blind placebo controlled trial of neoadjuvant clopidogrel and aspirin versus aspirin alone in patients undergoing angioplasty for claudication

Fowkes FGR, 0:

Randomised controlled trial of low dose aspirin in the prevention of cardiovascular events and death in subjects with asymptomatic atherosclerosis.

McCollum CN, 0:

The influence of antiplatelet therapy (clopidogrel) on biochemical response to intermittent claudication

EUCLID, 2016:

Jones WS, Baumgartner I, Hiatt WR, Heizer G, Conte MS, White CJ, Berger JS, Held P, Katona BG, Mahaffey KW, Norgren L, Blomster J, Millegrd M, Reist C, Patel MR, Fowkes GR Ticagrelor Compared With Clopidogrel in Patients with Prior Lower Extremity Revascularization for Peripheral Artery Disease. Circulation 2016 Nov 13;: [27840336] 10.1161/CIRCULATIONAHA.116.025880

Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, Katona BG, Mahaffey KW, Norgren L, Jones WS, Blomster J, Millegrd M, Reist C, Patel MR Ticagrelor versus Clopidogrel in Symptomatic Peripheral Artery Disease. N Engl J Med 2017;376:32-40 [27959717]

Hess (2), 1985:

Drug-induced inhibition of platelet function delays progression of peripheral occlusive arterial disease. A prospective double-blind arteriographically controlled trial. Hess H, Mietaschk A, Deichsel G Lancet 1985 Feb 23;1:415-9 [2857803]

Schoop (2), 1983:

W Schoop, H Levy. prevention of peripheral arterial occlusive disease with antiaggregants. Thromb Haemost 1983, 30: 137.

VA study, 1986:

Veterans Administration Cooperative Study on antiplatelet agents in diabetic patients after amputation for gangrene: II. Effects of aspirin and dipyridamole on atherosclerotic vascular disease rates. Colwell JA, Bingham SF, Abraira C, Anderson JW, Comstock JP, Kwaan HC, Nuttall F Diabetes Care 1986 Mar-Apr;9:140-8 [3516608]

CLIPS, 2007:

Catalano M, Born G, Peto R Prevention of serious vascular events by aspirin amongst patients with peripheral arterial disease: randomized, double-blind trial. J Intern Med 2007 Mar;261:276-84 [17305650]

Munich B, 1975:

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration BMJ 2002 Jan 12;324:71-86 [11786451]

Munich A, 1975:

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration BMJ 2002 Jan 12;324:71-86 [11786451]

Schoop, 1983:

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration BMJ 2002 Jan 12;324:71-86 [11786451]

Hess, 1985:

Drug-induced inhibition of platelet function delays progression of peripheral occlusive arterial disease. A prospective double-blind arteriographically controlled trial. Hess H, Mietaschk A, Deichsel G Lancet 1985 Feb 23;1:415-9 [2857803]

CRAMPS, 2000:

Gresele P, Migliacci R, Di Sante G, Nenci GG; CRAMPS Investigator Group. Effect of cloricromene on intermittent claudication. A randomized, double-blind, placebo-controlled trial in patients treated with aspirin: effect on claudication distance and quality of life. CRAMPS Investigator Group. Cloricromene Randomized Arteriopathy Multicenter Prospective Study. Vasc Med 2000;5:83-9

Thulesius, 1987:

Ketanserin in intermittent claudication: effect on walking distance, blood pressure, and cardiovascular complications. Thulesius O, Lundvall J, Kroese A, Stranden E, Hallbook T, Brunes L, Gjores JE, Akesson H, Einarsson E, Ohlin P, et al J Cardiovasc Pharmacol 1987 Jun;9:728-33 [2442541]

Walden, 1991:

Randomized placebo-controlled, double-blind trial of ketanserin in treatment of intermittent claudication. Walden R, Bass A, Rabi I, Adar R J Cardiovasc Surg (Torino) 1991 Nov-Dec;32:737-40 [1752890]

PACK, 1996:

The PACK trial: morbidity and mortality effects of ketanserin. Prevention of Atherosclerotic Complications. Verstraete M Vasc Med 1996;1:135-40 [9546928]

Prevention of atherosclerotic complications: controlled trial of ketanserin. Prevention of Atherosclerotic Complications with Ketanserin Trial Group. BMJ 1989 Feb 18;298:424-30 [2495049]

Coto, 1989:

Clinical efficacy of picotamide in long-term treatment of intermittent claudication. Coto V, Cocozza M, Oliviero U, Lucariello A, Picano T, Coto F, Cacciatore L Angiology 1989 Oct;40:880-5 [2679241]

ADEP, 1993:

Effects of picotamide, an antiplatelet agent, on cardiovascular, events in 438 claudicant patients with diabetes: a retrospective analysis of the ADEP study. Milani M, Longoni A, Maderna M Br J Clin Pharmacol 1996 Dec;42:782-5 [8971437]

Effect of picotamide on the clinical progression of peripheral vascular disease. A double-blind placebo-controlled study. The ADEP Group. Balsano F, Violi F Circulation 1993 May;87:1563-9 [8491012]

Neirotti, 1994:

Hemodynamic, hemorheologic, and hemocoagulative changes after treatment with picotamide in patients affected by peripheral arterial disease (PAD) of the lower limbs. Neirotti M, Molaschi M, Ponzetto M, Macchione C, Poli L, Bonino F, Fabris F Angiology 1994 Feb;45:137-41 [8129189]

Adriaensen, 1976:

Medical treatment of intermittent claudication: a comparative double-blind study of suloctidil, dihydroergotoxine and placebo. Adriaensen H Curr Med Res Opin 1976;4:395-401 [793778]

Verhaeghe, 1981:

Controlled trial of suloctidil in intermittent claudication. Verhaeghe R, Van Hoof A, Beyens G J Cardiovasc Pharmacol 1981 Mar-Apr;3:279-86 [6166799]

Jones, 1982:

A double-blind trial of suloctidil v. placebo in intermittent claudication. Jones NA, De Haas H, Zahavi J, Kakkar VV Br J Surg 1982 Jan;69:38-40 [6274471]

Holm, 1984:

Intermittent claudication: Suloctidil v.s. placebo treatment. Holm J, Lindblad L, Schersten T, Suurkula M Vasa 1984;13:175-8 [6331019]

Ellis, 1986:

DJ Ellis, BR Kamm. Treatment of intermittent claudication with Ticlopidine. Institute of Clinical Medicine, Syntex Research. Palo Alto.CA 94304, USA. Modifier — Effacer — pdf

Hurlow, 1980:

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration BMJ 2002 Jan 12;324:71-86 [11786451]

Krause, 1980:

Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration BMJ 2002 Jan 12;324:71-86 [11786451]

Katsumara, 1982:

Therapeutic effect of ticlopidine, a new inhibitor of platelet aggregation, on chronic arterial occlusive diseases, a double-blind study versus placebo. Katsumura T, Mishima Y, Kamiya K, Sakaguchi S, Tanabe T, Sakuma A Angiology 1982 Jun;33:357-67 [7046521]

Aukland, 1982:

Platelet inhibition with Ticlopidine in atherosclerotic intermittent claudication. Aukland A, Hurlow RA, George AJ, Stuart J J Clin Pathol 1982 Jul;35:740-3 [7047575]

Stiegler, 1984:

H Stiegler, H Hess, A Mietaschk, H-J, Trampisch and Ingrisch. DMW 1984, 109:1240-1243.

Cloarec, 1986:

Cloarec M et al Double-blind clinical trial of ticlopidine versus placebo in peripheral atherosclerotic disease of the legs Thrombosis Research 1986 suppl VI abstr 316

Arcan, 1988:

Multicenter double-blind study of ticlopidine in the treatment of intermittent claudication and the prevention of its complications. Arcan JC, Blanchard J, Boissel JP, Destors JM, Panak E Angiology 1988 Sep;39:802-11 [3048155]

Balsano, 1989:

Ticlopidine in the treatment of intermittent claudication: a 21-month double-blind trial. Balsano F, Coccheri S, Libretti A, Nenci GG, Catalano M, Fortunato G, Grasselli S, Violi F, Hellemans H, Vanhove P J Lab Clin Med 1989 Jul;114:84-91 [2661700]

STIMS, 1990:

Prevention of myocardial infarction and stroke in patients with intermittent claudication; effects of ticlopidine. Results from STIMS, the Swedish Ticlopidine Multicentre Study. Janzon L, Bergqvist D, Boberg J, Boberg M, Eriksson I, Lindgarde F, Persson G, Almgren B, Fagher B, Kjellstrom T, et al J Intern Med 1990 May;227:301-8 [2187948]

EMATAP, 1993:

J Blanchard, LO Carrerars, M Kindermans and the EMATAP group. Results of EMATAP: a dooble-blind placebo-controlled multicentre trial of ticlopidine in patients with peripheral arterial disease. Nouv Rev fr Hematol(1993)35:523-528.

CAPRIE, 1996:

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39 [8918275]

CAPRIE, 1996:

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39 [8918275]

3 selective PAR-1 thrombin receptor antagonist

Trial	Treatments	Patients	Trials design and methods
vorapaxar vs placebo (on top aspirin)			
TRA-2P TIMI 50 , 2012 [NCT00526474] n=13225/13244 follow-up: 2.5 y (median)	vorapaxar (SCH 530348) 2.5-mg daily versus placebo (added to the existing standard of care for preventing heart attack and stroke (eg, aspirin, clopidogrel)	patients with a known history of atherosclerosis (MI, ischemic stroke, or peripheral vascular disease)	Parallel groups double-blind

References

TRA-2P TIMI 50, 2012:

Morrow DA, Scirica BM, Fox KA, Berman G, Strony J, Veltri E, Bonaca MP, Fish P, McCabe CH, Braunwald E Evaluation of a novel antiplatelet agent for secondary prevention in patients with a history of atherosclerotic disease: design and rationale for the Thrombin-Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events (TRA 2

degrees P)-TIMI 50 trial. Am Heart J 2009 Sep;158:335-341.e3 [19699854]

Morrow DA, Braunwald E, Bonaca MP, Ameriso SF, Dalby AJ, Fish MP, Fox KA, Lipka LJ, Liu X, Nicolau JC, Oude Ophuis AJ, Paolasso E, Scirica BM, Spinar J, Theroux P, Wiviott SD, Strony J, Murphy SA Vorapaxar in the Secondary Prevention of Atherothrombotic Events. N Engl J Med 2012 Mar 24;: [22443427] 10.1056/NEJMoa1200933

Scirica BM, Bonaca MP, Braunwald E, De Ferrari GM, Isaza D, Lewis BS, Mehrhof F, Merlini PA, Murphy SA, Sabatine MS, Tendera M, Van de Werf F, Wilcox R, Morrow DA Vorapaxar for secondary prevention of thrombotic events for patients with previous myocardial infarction: a prespecified subgroup analysis of the TRA 2P-TIMI 50 trial. Lancet 2012;380:1317-24 [22932716]

4 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.