Clinical trials of antithrombotics for cardiovascular prevention in all type of patients

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1 anticoagulant

Trial	Treatments	Patients	Trials design and methods
warfarin vs placebo			
Thrombosis Prevention trial (Warfarin) , 1998 [NCT00000614] n=2762/2737 follow-up: median 6.8 y	warfarin started at 2.5mg/d adjusted for a target INR 1.5 versus placebo	men aged between 45 years and 69 years at high risk of IHD	Factorial plan double blind UK

References

Thrombosis Prevention trial (Warfarin), 1998:

Thrombosis prevention trial: randomised trial of low-intensity oral anticoagulation with warfarin and low-dose aspirin in the primary prevention of ischaemic heart disease in men at increased risk. The Medical Research Council's General Practice Research Framework. Lancet 1998;351:233-41 [9457092]

Meade TW, Wilkes HC, Stirling Y, Brennan PJ, Kelleher C, Browne W Randomized controlled trial of low dose warfarin in the primary prevention of ischaemic heart disease in men at high risk: design and pilot study. Eur Heart J 1988;9:836-43 [3053176]

Meade TW, Roderick PJ, Brennan PJ, Wilkes HC, Kelleher CC Extra-cranial bleeding and other symptoms due to low dose aspirin and low intensity oral anticoagulation. Thromb Haemost 1992;68:1-6 [1514166]

2 anticoagulant + antiplatelet

Trial	Treatments	Patients	Trials design and methods
warfarin + aspirin vs placebo			
Thrombosis Prevention trial (W plus A) , 1998 [NCT00000614] n=1277/1272 follow-up: median 6.8 y	warfarin adjusted dose for INR of 1.5 + aspirin 75 mg daily versus placebo	men aged between 45 years and 69 years at high risk of IHD	NA double blind UK

References

Thrombosis Prevention trial (W plus A), 1998:

Thrombosis prevention trial: randomised trial of low-intensity oral anticoagulation with warfarin and low-dose aspirin in the primary prevention of ischaemic heart disease in men at increased risk. The Medical Research Council's General Practice Research Framework. Lancet 1998;351:233-41 [9457092]

Meade TW, Wilkes HC, Stirling Y, Brennan PJ, Kelleher C, Browne W Randomized controlled trial of low dose warfarin in the primary prevention of ischaemic heart disease in men at high risk: design and pilot study. Eur Heart J 1988;9:836-43 [3053176]

3 NOAC

Trial	Treatments	Patients	Trials design and methods
rivaroxaban vs aspirin			
COMPASS (rivaroxaban alone) *ongoing* [NCT01776424] n=27400 follow-up:	Rivaroxaban 2.5 mg twice daily alone versus aspirin 100 mg once daily	Patients With Coronary or Peripheral Artery Disease	
rivaroxaban + aspirin vs aspirin			
COMPASS (rivaroxaban + aspirin) *ongoing* [NCT01776424] n=27400 follow-up:	versus aspirin 100 mg once daily	Patients With Coronary or Peripheral Artery Disease	

References

COMPASS (rivaroxaban alone), :
COMPASS (rivaroxaban + aspirin), 0:

4 P2Y12 receptor-antagonist

Trial	Treatments	Patients	Trials design and methods
ticagrelor vs placebo (on top aspirin)			
PEGASUS 90mg , 2015 [NCT01225562] n=7050/7067 follow-up: 2.75 y (median)	-	patients who had had a myocardial infarction 1 to 3 years earlier	double-blind
PEGASUS 60mg , 2015 [NCT01225562] n=7045/7067 follow-up: 2.75 y (median)	ticagrelor at a dose of 60 mg twice daily versus placebo	patients who had had a myocardial infarction 1 to 3 years earlier	Parallel groups double-blind

References

PEGASUS 90mg, 2015:

Bonaca MP, Bhatt DL, Braunwald E, Cohen M, Steg PG, Storey RF, Held P, Jensen EC, Sabatine MS Design and rationale for the Prevention of Cardiovascular Events in

Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial. Am Heart J 2014;167:437-444.e5 [24655690]

Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Ophuis TO, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N Engl J Med 2015 Mar 14;: [25773268] 10.1056/NEJMoa1500857

PEGASUS 60mg, 2015:

Bonaca MP, Bhatt DL, Braunwald E, Cohen M, Steg PG, Storey RF, Held P, Jensen EC, Sabatine MS Design and rationale for the Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial. Am Heart J 2014;167:437-444.e5 [24655690]

Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Ophuis TO, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N Engl J Med 2015 Mar 14;: [25773268] 10.1056/NEJMoa1500857

5 platelet aggregation inhibitors

Trial	Treatments	Patients	Trials design and methods
aspirin vs no treatment			
British Doctors Trial , 1988 n=3429/1710 follow-up: 5.5 years	aspirin 500 mg/d versus no aspirin	apparently healthy male doctors	Parallel groups open UK
Primary Prevention Project , 2001 n=2226/2269 follow-up: 3.6 y	aspirin 100 mg/d versus no aspirin (open control)	men and women aged 50 years or greater, with at least one of the major recognised cardiovascular risk factors.	Factorial plan Open Italy
aspirin vs placebo			
AAA , 2009 [ISRCTN66587262] n=1675/1675 follow-up: 8.2 y (mean)	aspirin 100mg daily versus placebo	men and women aged 50 to 80 years with asymptomatic atherosclerosis detected by low ankle brachial index (<=0.95)	Parallel groups double blind UK, Scotland
Physicians Health Study , 1989 [NCT00000500] n=11037/11034 follow-up: 60.2 months	aspirin 325 mg every other day versus placebo	Healthy men	Parallel groups double blind
Thrombosis Prevention Trial , 1998 [NCT00000614] n=2545/2540 follow-up: median 6.8y	aspirin 75 mg/d (controlled release) versus placebo	Men at high risk of CHD	Factorial plan double blind UK

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Trial	Treatments	Patients	Trials design and methods
HOT , 1998 n=9399/9391 follow-up: mean 3.8 y (range 3.3-4.9y)	aspirin 75 mg daily versus placebo	patients aged 50-80 with hypertension and diastolic blood pressure between 100 mmHG and 115 mmHG	Factorial plan Double blind Europe, North and South America, and Asia
Womens Health Study , 2005 n=19934/19942 follow-up: 10.1 y mean (range 8.2 to 10.9	aspirin 100mg daily versus placebo	initially healthy women 45 years of age or older	Factorial plan Double blind

References

British Doctors Trial, 1988:

Peto R, Gray R, Collins R, Wheatley K, Hennekens C, Jamrozik K, Warlow C, Hafner B, Thompson E, Norton S Randomised trial of prophylactic daily aspirin in British male doctors. Br Med J (Clin Res Ed) 1988 Jan 30;296:313-6 [3125882]

Primary Prevention Project, 2001:

de Gaetano G Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001 Jan 13;357:89-95 [11197445]

AAA, 2009:

Fowkes FG, Price JF, Stewart MC, Butcher I, Leng GC, Pell AC, Sandercock PA, Fox KA, Lowe GD, Murray GD Aspirin for prevention of cardiovascular events in a general population screened for a low ankle brachial index: a randomized controlled trial. JAMA 2010 Mar 3;303:841-8 [20197530] 10.1001/jama.2010.221

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HOT, 1998:

Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Menard J, Rahn KH, Wedel H, Westerling S Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998 Jun 13;351:1755-62 [9635947]

Hansson L, Zanchetti A The Hypertension Optimal Treatment (HOT) Study–patient characteristics: randomization, risk profiles, and early blood pressure results. Blood Press 1994;3:322-7 [7866597]

Womens Health Study, 2005:

Ridker PM, Cook NR, Lee IM, Gordon D, Gaziano JM, Manson JE, Hennekens CH, Buring JE A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. N Engl J Med 2005 Mar 31;352:1293-304 [15753114]

Rexrode KM, Lee IM, Cook NR, Hennekens CH, Buring JE Baseline characteristics of participants in the Women's Health Study. J Womens Health Gend Based Med 2000;9:19-27 [10718501] 10.1089/152460900318911

6 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
TRA-2P TIMI 50 (no prior stroke sub group) , 2012 n=20699 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), sub group of patient with no prior stroke	Parallel groups double-blind
TRA-2P TIMI 50 (MI subgroup) , 2012 [NCT00526474] n=8898/8881 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)	prespecified subgroup of patients with a qualifying myocardial infarction among the overall population of patients with a known history of atherosclerosis (MI, ischemic stroke, or peripheral vascular disease)	Parallel groups double-blind multinational

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]

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TRA-2P TIMI 50 (no prior stroke sub group), 2012:

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

TRA-2P TIMI 50 (MI subgroup), 2012:

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

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7 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

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