

Clinical trials of antithrombotics for venous thrombosis in secondary prevention of VTE

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1 anticoagulant

Trial	Treatments	Patients	Trials design and methods
warfarin vs discontinuation			
PROLONG (Palareti) , 2006 [NCT00264277] n=105/122 follow-up: 1.4 yeras	prolongation versus no anticoagulation	patients with an abnormal d-dimer level 1 month after the discontinuation of anticoagulation in patients with a first unprovoked proximal deep-vein thrombosis or pulmonary embolism who had received a vitamin K antagonist for at least 3 months	Parallel groups
PREVENT (Ridker) , 2003 n=255/253 follow-up: 2.1 years	extension with low-intensity warfarin (target INR, 1.5 to 2.0) versus placebo	Patients with idiopathic venous thromboembolism who had received full-dose anticoagulation therapy for a median of 6.5 months	Parallel groups
Agnelli , 2003 n=NA follow-up: 33 months	continuation for 3 or 9 additionnal months of warfarin or other oral anticoagulant was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding after a first episode of pulmonary embolism	Parallel groups open Italy
Agnelli , 2001 n=NA follow-up: 33 months	continuation for 9 additional months; warfarin or acenocoumarol adjusted to achieve a target INR between 2.0 and 3.0 versus discontinuation (after 3 months months)	Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy	Parallel groups open Italy
LAFIT (Kearon) , 1999 n=NA follow-up:	Continuation of the oral anticoagulant therapy up to 24 months, warfarin was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism	
Levine , 1995 n=NA follow-up: 11 months after randomization.	continuation for 2 months of warfarin adjusted INR value of 2.0 to 3.0 versus Discontinue oral anticoagulant therapy (after 1 months)	Patients with venographically confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal	Parallel groups double blind Canada, Italy

continued...

Trial	Treatments	Patients	Trials design and methods
DURAC (Schulman) , 1997 n=NA follow-up: Four years after randomization	indefinite warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85 versus 6 months warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85	-	Parallel groups open Sweden

References

PROLONG (Palareti), 2006:

Palareti G, Cosmi B, Legnani C, Tositto A, Brusi C, Iorio A, Pengo V, Ghirarduzzi A, Pattacini C, Testa S, Lensing AW, Tripodi A D-dimer testing to determine the duration of anticoagulation therapy. N Engl J Med 2006;355:1780-9 [[17065639](#)]

PREVENT (Ridker), 2003:

Ridker PM, Goldhaber SZ, Danielson E, Rosenberg Y, Eby CS, Deitcher SR, Cushman M, Moll S, Kessler CM, Elliott CG, Paulson R, Wong T, Bauer KA, Schwartz BA, Miletich JP, Bounameaux H, Glynn RJ Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. N Engl J Med 2003;348:1425-34 [[12601075](#)]

Agnelli, 2003:

Agnelli G, Prandoni P, Becattini C, Silingardi M, Taliani MR, Miccio M, Imberti D, Poggio R, Ageno W, Pogliani E, Porro F, Zonzin P Extended oral anticoagulant therapy after a first episode of pulmonary embolism. Ann Intern Med 2003;139:19-25 [[12834314](#)]

Agnelli, 2001:

Agnelli G, Prandoni P, Santamaria MG, Bagatella P, Iorio A, Bazzan M, Moia M, Guazzaloca G, Bertoldi A, Tomasi C, Scannapieco G, Ageno W Three months versus one year of oral anticoagulant therapy for idiopathic deep venous thrombosis. Warfarin Optimal Duration Italian Trial Investigators. N Engl J Med 2001;345:165-9 [[11463010](#)]

LAFIT (Kearon), 1999:

Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, Turpie AG, Green D, Ginsberg JS, Wells P, MacKinnon B, Julian JA A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. N Engl J Med 1999;340:901-7 [[10089183](#)]

Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, Turpie AG, Green D, Ginsberg JS, Wells P, MacKinnon B, Julian JA A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. N Engl J Med 1999;340:901-7 [[10089183](#)]

Levine, 1995:

Levine MN, Hirsh J, Gent M, Turpie AG, Weitz J, Ginsberg J, Geerts W, LeClerc J, Neemeh J, Powers P Optimal duration of oral anticoagulant therapy: a randomized trial comparing four weeks with three months of warfarin in patients with proximal deep vein thrombosis. Thromb Haemost 1995;74:606-11 [[8584992](#)]

DURAC (Schulman), 1997:

Schulman S, Granqvist S, Holmström M, Carlsson A, Lindmarker P, Nicol P, Eklund SG, Nordlander S, Lrfars G, Leijd B, Linder O, Loogna E The duration of oral anticoagulant therapy after a second episode of venous thromboembolism. The Duration of Anticoagulation Trial Study Group. N Engl J Med 1997;336:393-8 [[9010144](#)]

2 antiplatelet

Trial	Treatments	Patients	Trials design and methods
aspirin vs discontinuation			
WARFASA , 2012 [NCT00222677] n=205/197 follow-up: 24.6 mo (median)	aspirin, 100 mg daily for 2 years versus placebo	patients with first-ever unprovoked venous thromboembolism who had completed 6 to 18 months of oral anticoagulant treatment	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
ASPIRE , 2012 [ACTRN1260500004662] n=411/411 follow-up: 37.2 montsh (median)	-	patients who had completed initial anticoagulant therapy after a first episode of unprovoked venous thromboembolism	

References

WARFASA, 2012:

Becattini C, Agnelli G, Schenone A, Eichinger S, Bucherini E, Silingardi M, Bianchi M, Moia M, Ageno W, Vandelli MR, Grandone E, Prandoni P Aspirin for preventing the recurrence of venous thromboembolism. N Engl J Med 2012 May 24;366:1959-67 [[22621626](#)] [10.1056/NEJMoa1114238](#)

ASPIRE, 2012:

Brighton TA, Eikelboom JW, Mann K, Mister R, Gallus A, Ockelford P, Gibbs H, Hague W, Xavier D, Diaz R, Kirby A, Simes J Low-dose aspirin for preventing recurrent venous thromboembolism. N Engl J Med 2012;367:1979-87 [[23121403](#)]

3 direct anti-Xa

Trial	Treatments	Patients	Trials design and methods
apixaban 2.5mg vs discontinuation			
AMPLIFY-EXT 2.5mg , 2012 [NCT00633893] n=842/829 follow-up: 12 mo	Extended Treatment with apixaban 2.5 mg twice daily 12 months versus placebo	patients who have completed their intended treatment for deep vein thrombosis or pulmonary embolism	Parallel groups double blind
apixaban 5mg vs discontinuation			
AMPLIFY-EXT 5mg , 2012 [NCT00633893] n=815/829 follow-up: 12 mo	Extended Treatment with apixaban 5 mg twice daily 12 months versus placebo	patients who have completed their intended treatment for deep vein thrombosis or pulmonary embolism	double blind
rivaroxaban vs discontinuation			
EINSTEIN-extension , 2009 [NCT00439725] n=602/595 follow-up:	rivaroxaban 20 mg once-daily for an additional 6 or 12 months versus placebo	patients who had completed six to 12 months of anticoagulant treatment for an acute episode of VTE	Parallel groups double blind 28 countries

References

AMPLIFY-EXT 2.5mg, 2012:

Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Porcari A, Raskob GE, Weitz JI Apixaban for Extended Treatment of Venous Thromboembolism. N Engl J Med 2012 Dec 8; [[23216615](#)] [10.1056/NEJMoa1207541](#)

AMPLIFY-EXT 5mg, 2012:

Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Porcari A, Raskob GE, Weitz JI Apixaban for Extended Treatment of Venous Thromboembolism. N Engl J Med

2012 Dec 8;: [23216615] 10.1056/NEJMoa1207541

EINSTEIN-extension, 2009:

Biller H R. Once daily oral rivaroxaban versus placebo in the long term treatment of recurrent symptomatic venous thromboembolism. The Einstein-extension study. *ASH*, 8 dcembre 2009

Oral Rivaroxaban for Symptomatic Venous Thromboembolism. *N Engl J Med* 2010 Dec 3;: [21128814] 10.1056/NEJMoa1007903

4 oral direct thrombin inhibitor

Trial	Treatments	Patients	Trials design and methods
dabigatran vs warfarin			
RE-MEDY , 2011 [NCT00329238] n=1430/1426 follow-up: 6 to 36 months	dabigatran 150 mg twice daily for an additional period of 6 to 36 months versus warfarin (to maintain an international normalized ratio of 2.0 to 3.0) for an additional period of 6 to 36 months	Secondary prevention of VTE in patients with VTE who had initially received 3 to 12 months of anticoagulant therapy	Parallel groups double-blind
dabigatran vs discontinuation			
RE-SONATE , 2011 [NCT00558259] n=681/662 follow-up:	dabigatran 150 mg twice daily for an additional period of 6 months versus placebo	Secondary prevention of VTE in patients with VTE who had completed 6-18 months of anticoagulant therapy	Parallel groups double-blind
ximelagatran vs discontinuation			
THRIVE III , 2003 n=612/611 follow-up: 18 months	ximelagatran 24 mg twice daily for 18 months versus placebo for 18 months	patients with venous thromboembolism who had undergone six months of anticoagulant therapy	Parallel groups double blind 18 countries

References

RE-MEDY, 2011:

Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, Baanstra D, Kvamme AM, Friedman J, Mismetti P, Goldhaber SZ Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med* 2013 Feb 21;368:709-18 [23425163] 10.1056/NEJMoa1113697

RE-SONATE, 2011:

THRIVE III, 2003:

Schulman S, Whlander K, Lundstrm T, Clason SB, Eriksson H Secondary prevention of venous thromboembolism with the oral direct thrombin inhibitor ximelagatran. *N Engl J Med* 2003 Oct 30;349:1713-21 [14585939]

Schulman S, Lundstrm T, Wlander K, Billing Clason S, Eriksson H Ximelagatran for the secondary prevention of venous thromboembolism: a complementary follow-up analysis of the THRIVE III study. *Thromb Haemost* 2005 Oct;94:820-4 [16270637]

5 synthetic pentasaccharide

Trial	Treatments	Patients	Trials design and methods
idraparinux vs discontinuation			
VanGogh extension , 2007 [NCT00071279] n=594/621 follow-up: 6 months	once-weekly injections of 2.5 mg of idraparinux for 6 months versus placebo	patients who had completed 6 months of prophylaxis with idraparinux or a vitamin K antagonist and in whom extended anticoagulation was warranted	Parallel groups

References

VanGogh extension, 2007:

6 About TrialResults-center.org

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