

# Clinical trials of antithrombotics for venous thrombosis in secondary prevention - 2

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## 1 antiagregant

| Trial   | Treatments   | Patients  | Trials design and methods |
|---|--|---|---------------------------|
| <b>aspirin vs placebo</b>   |  |   |                           |
| <b>ASPIRE , 2012</b><br>n=411/411<br>follow-up: 37.2 months<br>median | aspirin, at a dose of 100 mg daily, for up to 4 years<br>versus<br>placebo | patients who had completed initial anticoagulant therapy after a first episode of unprovoked venous thromboembolism         |                           |
| <b>WARFASA , 2012</b><br>n=205/197<br>follow-up:                      | aspirin, 100 mg daily for 2 years<br>versus<br>placebo                     | patients with first-ever unprovoked venous thromboembolism who had completed 6 to 18 months of oral anticoagulant treatment |                           |

## References

### 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](#)] [10.1056/NEJMoa1210384](#)

### 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;366:1959-67 [[22621626](#)] [10.1056/NEJMoa1114238](#)

## 2 direct anti-IIa

| Trial   | Treatments  | Patients   | Trials design and methods |
|---|---|--|---------------------------|
| <b>dabigatran vs placebo</b>                      |   |  |                           |
| <b>RESONATE , 2013</b><br>n=681/662<br>follow-up: | dabigatran at a dose of 150 mg twice daily<br>versus<br>placebo | -  |                           |
| <b>ximelagatran vs placebo</b>                    |   |  |                           |
| <b>THRIVE 3 , 2003</b><br>n=612/611<br>follow-up: | ximelagatran (24 mg)<br>versus<br>placebo                       | patients with venous thromboembolism who had undergone six months of anticoagulant therapy |                           |
| <b>dabigatran vs warfarin</b>                     |   |  |                           |

continued...

| Trial   | Treatments | Patients | Trials design and methods |
|---|------------|----------|---------------------------|
| <b>REMEDY , 2013</b><br>n=1430/1426<br>follow-up: | -          | -        |                           |

## References

### RESONATE, 2013:

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

### THRIVE 3, 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;349:1713-21 [14585939] 10.1056/NEJMoa030104

### REMEDY, 2013:

Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, Baanstra D, Kvanme 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]

## 3 direct anti-Xa

2

| Trial  | Treatments  | Patients   | Trials design and methods |
|--|---|--|---------------------------|
| <b>rivaroxaban 10mg vs aspirin</b>   |   |  |                           |
| <b>EINSTEIN CHOICE (10mg) , 2017</b><br>[NCT02064439]<br>n=1127/1131<br>follow-up: | Rivaroxaban 10 mg once daily for 12 months versus<br>ASA (Acetylsalicylic Acid) 100 mg once daily for 12 months | Patients with confirmed symptomatic DVT (Deep Vein Thrombosis) or PE (Pulmonary embolism) who completed 6 or 12 months of treatment of anticoagulation |                           |
| <b>apixaban 2.5mg vs placebo</b>   |   |  |                           |
| <b>AMPLIFY EXT 2.5mg , 2013</b><br>n=842/829<br>follow-up:                         | apixaban (2.5 mg and 5 mg, twice daily) versus<br>placebo   | patients with venous thromboembolism who had completed 6 to 12 months of anticoagulation therapy   |                           |
| <b>apixaban 5mg vs placebo</b>   |   |  |                           |
| <b>AMPLIFY EXT 5mg , 2013</b><br>n=815/829<br>follow-up:                           | apixaban (2.5 mg and 5 mg, twice daily) versus<br>placebo   | patients with venous thromboembolism who had completed 6 to 12 months of anticoagulation therapy   |                           |
| <b>rivaroxaban 20mg vs placebo</b>   |   |  |                           |
| <b>EISNTEIN EXT , 2010</b><br>n=602/595<br>follow-up:                              | rivaroxaban alone (20 mg once daily)for an additional 6 or 12 months versus<br>placebo                          | patients who had completed 6 to 12 months of treatment for venous thromboembolism  |                           |
| <b>rivaroxaban 20mg vs aspirin</b>   |   |  |                           |

continued...

| Trial  | Treatments  | Patients   | Trials design and methods |
|--|---|--|---------------------------|
| <b>EINSTEIN CHOICE (20mg) , 2017</b><br>[NCT02064439]<br>n=1107/1131<br>follow-up: | Rivaroxaban 20 mg once daily for 12 months<br>versus<br>ASA (Acetylsalicylic Acid) 100 mg once daily<br>for 12 months | Patients with confirmed symptomatic DVT (Deep Vein Thrombosis) or PE (Pulmonary embolism) who completed 6 or 12 months of treatment of anticoagulation |                           |

## References

### **EINSTEIN CHOICE (10mg), 2017:**

Weitz JI, Lensing AWA, Prins MH, Bauersachs R, Beyer-Westendorf J, Bounameaux H, Brighton TA, Cohen AT, Davidson BL, Decousus H, Freitas MCS, Holberg Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism. N. Engl. J. Med. 2017; 376:1211-1222 [[28316279](#)] [10.1056/NEJMoa1700518](#)

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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 2013;368:699-708 [[23216615](#)] [10.1056/NEJMoa1207541](#)

### **AMPLIFY EXT 5mg, 2013:**

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 2013;368:699-708 [[23216615](#)] [10.1056/NEJMoa1207541](#)

### **EISNTEIN EXT, 2010:**

Bauersachs R, Berkowitz SD, Brenner B, Buller HR, Decousus H, Gallus AS, Lensing AW, Misselwitz F, Prins MH, Raskob GE, Segers A, Verhamme P, Wells P, Agnelli G, Bounameaux H, Cohen A, Davidson BL, Piovella F, Schellong S Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010;363:2499-510 [[21128814](#)] [10.1056/NEJMoa1007903](#)

### **EINSTEIN CHOICE (20mg), 2017:**

Weitz JI, Lensing AWA, Prins MH, Bauersachs R, Beyer-Westendorf J, Bounameaux H, Brighton TA, Cohen AT, Davidson BL, Decousus H, Freitas MCS, Holberg Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism. N. Engl. J. Med. 2017; 376:1211-1222 [[28316279](#)] [10.1056/NEJMoa1700518](#)

## 4 idraparinux

| Trial   | Treatments   | Patients   | Trials design and methods       |
|---|--|--|---------------------------------|
| <b>idraparinux vs placebo</b><br><b>Van Gogh , 2007</b><br>[NCT00071279]<br>n=594/621<br>follow-up: | once-weekly injections of 2.5 mg of idraparinux for 6 months without monitoring<br>versus<br>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<br>double-blind |

## References

### **Van Gogh, 2007:**

Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE Extended prophylaxis of venous thromboembolism with idraparinux. N Engl J Med 2007;357:1105-12 [[17855671](#)] [10.1056/NEJMoa067703](#)

## 5 VKA

| Trial  | Treatments   | Patients  | Trials design and methods     |
|--|--|---|-------------------------------|
| <b>VKA vs control</b>  |  |   |                               |
| <b>AUREC FVII , 2009</b><br>n=17/17<br>follow-up: 37 months mean                       | continue VKA for additional 24 months<br>versus<br>discontinuation   | patients with first spontaneous VTE and FVIII levels >230 IU/dl after 6 monthsh of VKA  |                               |
| <b>DACUS (Siragusa) , 2008</b><br>[NCT00438230]<br>n=88/92<br>follow-up:               | anticoagulants for 9 additional months<br>versus<br>no treatment   | with a first episode of deep vein thrombosis, treated with OAT for 3 months and with Residual vein thrombosis   |                               |
| <b>DURAC II , 1997</b><br>n=116/111<br>follow-up: 4 years                              | anticoagulant therapy continued indefinitely<br>versus<br>six months of oral anticoagulant therapy   | patients who had had a second episode of venous thromboembolism   |                               |
| <b>PROLONG (Palarati) , 2006</b><br>[NCT00264277]<br>n=105/122<br>follow-up: 1.4 years | resume treatment<br>versus<br>discontinue treatment  | patients with a first unprovoked proximal deep-vein thrombosis or pulmonary embolism who had received a vitamin K antagonist for at least 3 months and with abnormal D-dimer testing 1 month after the discontinuation of anticoagulation |                               |
| <b>WODIT DVT , 2001</b><br>n=134/133<br>follow-up: at least two years                  | continuation for nine additional months<br>versus<br>discontinuation   | Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy  |                               |
| <b>WODIT PE , 2003</b><br>n=165/161<br>follow-up:                                      | -  | patients after a first episode of pulmonary embolismwho had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding  |                               |
| <b>DDOAT2006 ongoing</b><br>[NCT00895505]<br>n=300<br>follow-up: 24 months             | Extension of OAT<br>versus<br>discontinuation  | -   |                               |
| <b>warfarin vs control</b>   |  |   |                               |
| <b>Vitotec , 2009</b><br>n=27/25<br>follow-up:   | continuation of warfarin for another 6 months<br>versus<br>discontinuation of warfarin   | patients with idiopathic DVT After 6 months of standard therapy (heparin/LMWH, warfarin with target INR 2-3) and persistent echogenic masses of over 20% of venous diameter   |                               |
| <b>warfarin vs low intensity warfarin</b>  |  |   |                               |
| <b>ELATE , 2003</b><br>n=369/369<br>follow-up: 2.4 years mean                          | continue warfarin therapy with a target international normalized ratio (INR) of 2.0 to 3.0<br>versus<br>target INR of 1.5 to 1.9 (low intensity) | patients who had completed three or more months of warfarin therapy for unprovoked venous thromboembolism   | Parallel groups<br>open-label |
| <b>low-intensity warfarin vs placebo</b>   |  |   |                               |

continued...

| Trial  | Treatments  | Patients   | Trials design and methods |
|--|---|--|---------------------------|
| <b>PREVENT , 2003</b><br>n=255/253<br>follow-up: 2.1 years mean                | low-intensity warfarin (target INR, 1.5 to 2.0)<br>versus<br>placebo  | Patients with idiopathic venous thromboembolism who had received full-dose anticoagulation   | double-blind              |
| <b>VKA vs placebo</b>  |   |  |                           |
| <b>PADIS-PE (Couturaud) , 2015</b><br>[NCT00740883]<br>n=184/187<br>follow-up: | additional 18-month treatment with warfarin<br>versus<br>placebo  | patients who had experienced a first episode of symptomatic unprovoked pulmonary embolism (ie, with no major risk factor for thrombosis) and had been treated initially for 6 uninterrupted months with a vitamin K antagonist | double-blind              |
| <b>warfarin vs placebo</b>   |   |  |                           |
| <b>LAFIT , 1999</b><br>n=79/83<br>follow-up: 10 months                         | warfarin for a further 24 months<br>versus<br>placebo   | patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism  | double-blind              |
| <b>Levine , 1995</b><br>n=109/105<br>follow-up:                                | continue warfarin (targeted International Normalized Ratio 2.0 to 3.0) for a further eight weeks<br>versus<br>placebo | Patients with venographically confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal  |                           |

## References

### AUREC FVII, 2009:

Eischer L, Gartner V, Schulman S, Kyrle PA, Eichinger S 6 versus 30 months anticoagulation for recurrent venous thrombosis in patients with high factor VIII. *Ann Hematol* 2009;88:485-90 [[18931845](#)] [10.1007/s00277-008-0626-1](#)

### DACUS (Siragusa), 2008:

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### PROLONG (Palarati), 2006:

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### WODIT PE, 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](#)]

### DDOAT2006, :

**Vitotec, 2009:**

Vtovec M, Goln L, Roztocil K, Linhart A The development of persistent thrombotic masses in patients with deep venous thrombosis randomized to long-term anticoagulation treatment. *Vasa* 2009;38:238-44 [[19736635](#)] [10.1024/0301-1526.38.3.238](#)

**ELATE, 2003:**

Kearon C, Ginsberg JS, Kovacs MJ, Anderson DR, Wells P, Julian JA, MacKinnon B, Weitz JI, Crowther MA, Dolan S, Turpie AG, Geerts W, Solymoss S, van Nguyen P, Demers C, Kahn SR, Kassis J, Rodger M, Hambleton J, Gent M Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. *N Engl J Med* 2003;349:631-9 [[12917299](#)] [10.1056/NEJMoa035422](#)

**PREVENT, 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](#)] [10.1056/NEJMoa035029](#)

**PADIS-PE (Couturaud), 2015:**

Couturaud F, Sanchez O, Pernod G, Mismetti P, Jego P, Duhamel E, Provost K, dit Sollier CB, Presles E, Castellant P, Parent F, Salaun PY, Bressollette L, Nonent M, Lorillon P, Girard P, Lacut K, Gugan M, Bosson JL, Laporte S, Leroyer C, Dcousus H, Meyer Six Months vs Extended Oral Anticoagulation After a First Episode of Pulmonary Embolism: The PADIS-PE Randomized Clinical Trial. *JAMA* 2015;314:31-40 [[26151264](#)] [10.1001/jama.2015.7046](#)

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## 6 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.

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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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