

# Clinical trials of direct oral anticoagulant (DAO) for DVT prophylaxis in orthopaedic surgery

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 direct factor Xa inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>apixaban vs enoxaparin</b>			
<b>ADVANCE 3 , 2010</b> [NCT00423319] n=2708/2699 follow-up: 35 days (+60)	apixaban 2.5mg twice daily for 35 days versus enoxaparin 40mg once daily for 35 days	patients undergoing elective total hip replacement surgery	Parallel groups double blind 21 countries
<b>rivaroxaban vs enoxaparin</b>			
<b>RECORD 1 , 2008</b> [NCT00329628] n=2266/2275 follow-up: 36 days (range 30-42)	rivaroxaban 10mg once daily for 35 days versus enoxaparin 40mg subcutaneous once daily for 31-39 days	patients undergoing total hip arthroplasty	Parallel groups double blind 27 countries worldwide
<b>apixaban vs enoxaparin (europe regimen)</b>			
<b>ADVANCE 2 , 2010</b> [NCT00452530] n=1528/1529 follow-up: 12 days	apixaban 2.5mg twice daily during 12 days versus enoxaparin 40mg once daily 12 days	patients undergoing elective unilateral or bilateral total knee replacement	Parallel groups double blind 27 countries
<b>rivaroxaban vs enoxaparin (europe regimen)</b>			
<b>RECORD 3 , 2008</b> [NCT00361894] n=1254/1277 follow-up: 13-17 days	rivaroxaban 10 mg once daily for 10- 14 days versus enoxaparin 40 mg subcutaneous once daily for 10-14 days	patients undergoing total knee arthroplasty	Parallel groups double blind 19 countries worldwide
<b>edoxaban vs enoxaparin (short duration)</b>			
<b>STARS J-V</b> [NCT01181167] n=255/248 follow-up:	edoxaban 30 mg once daily for 11 to 14 days versus subcutaneous enoxaparin 2,000 IU, equivalent to 20 mg, twice daily (BID) for 11 to 14 days	total hip arthroplasty	Parallel groups double-blind japan
<b>rivaroxaban vs enoxaparin (short duration)</b>			
<b>ODIXa-HIP 10mg , 2006</b> n=142/157 follow-up: 5-9 days	rivaroxaban 10mg daily for 59 days versus once-daily subcutaneous enoxaparin dose of 40 mg for 59 days	patients undergoing elective total hip replacement	Parallel groups double blind Europe, Israel
<b>rivaroxaban (long duration) vs enoxaparin (short duration)</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>RECORD 2 , 2008</b> [NCT00332020] n=1252/1257 follow-up: 30-42 days	extended thromboprophylaxis with rivaroxaban 10mg once daily for 31-39 days versus enoxaparin 40mg subcutaneous once daily for 10-14 days	patients undergoing elective total hip replacement	Parallel groups double blind 21 countries worldwide
<b>apixaban vs enoxaparin (US regimen)</b>			
<b>APROPOS 2.5mg , 2007</b> [NCT00097357] n=153/152 follow-up: 12 days	apixaban 2.5mg BID for 12 days versus enoxaparin 30mg twice daily for 12 days	patients undergoing elective total knee replacement surgery	Parallel groups double blind
<b>ADVANCE-1 , 2008</b> [NCT00371683] n=1599/1596 follow-up: 10-14 days	apixaban 2.5 mg orally twice daily for 10 to 14 days versus enoxaparin 30mg subcutaneously every 12 hours for 10-14 days	patients undergoing knee-replacement surgery	Parallel groups double blind 14 countries
<b>rivaroxaban vs enoxaparin (US regimen)</b>			
<b>ODIXa-KNEE , 2005</b> n=102/105 follow-up: 5-9 days	BAY 59-7939 5mg b.i.d. for 59 days versus enoxaparin 30 mg b.i.d. for 59 days	patients undergoing elective total knee replacement	Parallel groups double blind North America
<b>RECORD 4 , 2009</b> [NCT00362232] n=1584/1564 follow-up: 40 days	rivaroxaban 10mg once daily for 10 to 14 days versus enoxaparin 30 mg twice daily by subcutaneous injection for 10-14 days	patients who had undergone total-knee-replacement surgery	Parallel groups double blind 12 countries

2

## References

### ADVANCE 3, 2010:

Lassen MR, Gallus A, Raskob GE, Pineo G, Chen D, Ramirez LM Apixaban versus Enoxaparin for Thromboprophylaxis after Hip Replacement. N Engl J Med 2010;363:2487-2498 [21175312] [10.1056/NEJMoa1006885](https://doi.org/10.1056/NEJMoa1006885)

### RECORD 1, 2008:

Eriksson BI, Borris LC, Friedman RJ, Haas S, Huisman MV, Kakkar AK, Bandel TJ, Beckmann H, Muehlhofer E, Misselwitz F, Geerts W Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty N Engl J Med 2008;358:2765-75 [18579811] [10.1056/NEJMoa0800374](https://doi.org/10.1056/NEJMoa0800374)

### ADVANCE 2, 2010:

Lassen MR, Raskob GE, Gallus A, Pineo G, Chen D, Hornick P Apixaban versus enoxaparin for thromboprophylaxis after knee replacement (ADVANCE-2): a randomised double-blind trial. Lancet 2010 Mar 6;375:807-15 [20206776] [10.1016/S0140-6736\(09\)62125-5](https://doi.org/10.1016/S0140-6736(09)62125-5)

### RECORD 3, 2008:

Lassen MR, Ageno W, Borris LC, Lieberman JR, Rosencher N, Bandel TJ, Misselwitz F, Turpie AG Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. N Engl J Med 2008 Jun 26;358:2776-86 [18579812]

### STARS J-V, 0:

### ODIXa-HIP 10mg, 2006:

Eriksson BI, Borris L, Dahl OE, Haas S, Huisman MV, Kakkar AK, Misselwitz F, Klebo P Oral, direct Factor Xa inhibition with BAY 59-7939 for the prevention of venous thromboembolism after total hip replacement. J Thromb Haemost 2006 Jan;4:121-8 [16409461]

Eriksson BI, Borris LC, Dahl OE, Haas S, Huisman MV, Kakkar AK, Muehlhofer E, Dierig C, Misselwitz F, Klebo P A once-daily, oral, direct Factor Xa inhibitor, rivaroxaban (BAY 59-7939), for thromboprophylaxis after total hip replacement. *Circulation* 2006 Nov 28;114:2374-81 [17116766]

**RECORD 2, 2008:**

Kakkar AK, Brenner B, Dahl OE, Eriksson BI, Mouret P, Muntz J, Soglian AG, Pap AF, Misselwitz F, Haas S Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet* 2008 Jun 24;: [18582928]

**APROPOS 2.5mg, 2007:**

Lassen MR, Davidson BL, Gallus A, Pineo G, Ansell J, Deitchman D The efficacy and safety of apixaban, an oral, direct factor Xa inhibitor, as thromboprophylaxis in patients following total knee replacement. *J Thromb Haemost* 2007 Dec;5:2368-75 [17868430]

**ADVANCE-1, 2008:**

Lassen MR, Raskob GE, Gallus A, Pineo G, Chen D, Portman RJ Apixaban or enoxaparin for thromboprophylaxis after knee replacement. *N Engl J Med* 2009;361:594-604 [19657123]

**ODIXa-KNEE, 2005:**

Turpie AG, Fisher WD, Bauer KA, Kwong LM, Irwin MW, Klebo P, Misselwitz F, Gent M BAY 59-7939: an oral, direct factor Xa inhibitor for the prevention of venous thromboembolism in patients after total knee replacement. A phase II dose-ranging study. *J Thromb Haemost* 2005 Nov;3:2479-86 [16241946]

**RECORD 4, 2009:**

Turpie AG, Lassen MR, Davidson BL, Bauer KA, Gent M, Kwong LM, Cushner FD, Lotke PA, Berkowitz SD, Bandel TJ, Benson A, Misselwitz F, Fisher WD Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. *Lancet* 2009 May 16;373:1673-80 [19411100] 10.1016/S0140-6736(09)60734-0

## 2 oral direct thrombin inhibitor

33

Trial	Treatments	Patients	Trials design and methods
<b>dabigatran 150mg vs enoxaparin</b>			
RE-NOVATE (150mg) , 2007 [NCT00168818] n=1174/1162 follow-up: 28-35 days, median 33d	dabigatran etexilate 150 mg q.d. 28-35 days versus Enoxaparin 40 mg q.d. for 28-25 days	Total hip replacement	double blind Europe, Australia, South Africa
<b>dabigatran 220mg vs enoxaparin</b>			
RE-NOVATE 2 <i>unpublished</i> [NCT00657150] n=1010/1003 follow-up: 28-35 days (mean 32d)	dabigatran 220mg once daily for 28-35 Days versus enoxaparin 40mg subcutaneous once daily for 28-35 Days	patients undergoing total hip-replacement surgery	Parallel groups double-blind
RE-NOVATE (220mg) , 2007 [NCT00168818] n=1157/1162 follow-up: 28-35 days, median 33d	dabigatran etexilate 220 mg q.d. for 28-35 days versus Enoxaparin 40 mg q.d. for 23-35 days	Total hip replacement	Parallel groups double blind Europe, Australia, South Africa
<b>dabigatran 150mg vs enoxaparin (europe regimen)</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>RE-MODEL (150mg) , 2007</b> n=708/699 follow-up: 6-10 days, mean 8 days	dabigatran etexilate 150 mg q.d. for 6-10 days versus Enoxaparin 40 mg q.d. for 6-10 days	Total knee replacement	Parallel groups double blind Europe, Australia, South Africa
<b>dabigatran 220mg vs enoxaparin (europe regimen)</b>			
<b>RE-MODEL (220mg) , 2007</b> n=694/699 follow-up: 6-10 days, mean 8 days	dabigatran etexilate 220 mg q.d. 6-10 days versus Enoxaparin 40 mg q.d. for 6-10 days	patients undergoing total knee replacement	double blind Europe, Australia, South Africa
<b>dabigatran 150mg vs enoxaparin (US regimen)</b>			
<b>RE-MOBILIZE (150mg) , 2008</b> n=877/876 follow-up: 12-15 days, median 14d	dabigatran etexilate 150 mg q.d. for 12-15 days versus enoxaparin 30 mg SC BID after surgery for 12-15 days	Total knee replacement	double blind US, Canada, Mexico, UK
<b>dabigatran 220mg vs enoxaparin (US regimen)</b>			
<b>RE-MOBILIZE (220mg) , 2008</b> n=862/876 follow-up: 12-15 days, median 14d	dabigatran etexilate 220 mg for 12-15 days versus Enoxaparin 30mg SC BID after surgery for 12-15 days	Total knee replacement	Parallel groups double blind US, Canada, Mexico, UK

4

## References

### **RE-NOVATE (150mg), 2007:**

Eriksson BI, Dahl OE, Rosencher N, Kurth AA, van Dijk CN, Frostick SP, Prins MH, Hettiarachchi R, Hantel S, Schnee J, Bller HR Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. *Lancet* 2007;370:949-56 [[17869635](#)]

### **RE-NOVATE 2, 0:**

### **RE-NOVATE (220mg), 2007:**

Eriksson BI, Dahl OE, Rosencher N, Kurth AA, van Dijk CN, Frostick SP, Prins MH, Hettiarachchi R, Hantel S, Schnee J, Bller HR Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. *Lancet* 2007;370:949-56 [[17869635](#)]

### **RE-MODEL (150mg), 2007:**

Eriksson BI, Dahl OE, Rosencher N, Kurth AA, van Dijk CN, Frostick SP, Klebo P, Christiansen AV, Hantel S, Hettiarachchi R, Schnee J, Bller HR Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *J Thromb Haemost* 2007;5:2178-85 [[17764540](#)]  
[10.1111/j.1538-7836.2007.02748.x](#)

### **RE-MODEL (220mg), 2007:**

Eriksson BI, Dahl OE, Rosencher N, Kurth AA, van Dijk CN, Frostick SP, Klebo P, Christiansen AV, Hantel S, Hettiarachchi R, Schnee J, Bller HR Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *J Thromb Haemost* 2007 Nov;5:2178-85 [[17764540](#)]

### **RE-MOBILIZE (150mg), 2008:**

Ginsberg JS, Davidson BL, Comp PC, Francis CW, Friedman RJ, Huo MH, Lieberman JR, Muntz JE, Raskob GE, Clements ML, Hantel S, Schnee JM, Caprini JA Oral thrombin inhibitor dabigatran etexilate vs North American enoxaparin regimen for prevention of venous thromboembolism after knee arthroplasty surgery. *J Arthroplasty* 2009;24:1-9 [[18534438](#)]  
[10.1016/j.arth.2008.01.132](#)

**RE-MOBILIZE (220mg), 2008:**

The Oral Thrombin Inhibitor Dabigatran Etexilate vs the North American Enoxaparin Regimen for the Prevention of Venous Thromboembolism after Knee Arthroplasty Surgery. J Arthroplasty 2008;: [18534438]

### 3 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.