

Clinical trials of direct antithrombins for thrombosis prevention in orthopedic surgery

TrialResults-center www.trialresultscenter.org

1 oral direct thrombin inhibitor

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs Dalteparin			
METHRO I , 2002 n=103 follow-up: 69 days	Melagatran 14 mg s.c. immediately before surgery, melagatran at 20.00 hours, then ximelagatran 624 mg orally b.d. for 69 days versus Dalteparin 5000 IU o.d., started evening before surgery for 69 days	adults undergoing hip or knee replacement	parallel group open Swedish
METHRO II , 2002 n=1495/381 follow-up: 710 days	Melagatran 13 mg s.c. immediately before surgery, melagatran same day, then ximelagatran 824 mg orally b.d. for 710 days versus Dalteparin 5000 IU o.d., started evening before surgery for 710 days	undergoing hip or knee replacement	Parallel groups double-blind
ximelagatran vs Enoxaparin			
Platinum (Colwell) , 2003 n=906/910 follow-up: 712 days	Ximelagatran 24 mg orally b.d., starting at least 12 h after surgery for 712 days versus Enoxaparin 30 mg s.c. b.d., starting at least 12 h after surgery for 712 days	adults undergoing hip replacement	parallel group double-blind USA, Canada, Israel, Mexico, Argentina, South Africa
METHRO III , 2002 n=2788 follow-up: 811 days	Melagatran 3 mg s.c. 412h after surgery, then ximelagatran 24 mg orally b.d. for 710 days versus Enoxaparin 40 mg s.c. o.d. 12 h before surgery for 710 days	hip or knee replacement	double-blind Europe, South Africa
Phase II (Heit) , 2001 n=600 follow-up: 612 days	Ximelagatran 8, 12, 18 or 24 mg orally b.d., at least 12 h after surgery for 612 days versus Enoxaparin 30 mg s.c. b.d., starting at least 12 h after surgery for 612 days	adults (age > 18 years and weight at least 40 kg) undergoing knee replacements	parallel group double-blind North American
EXPRESS , 2003 n=2835 follow-up: 811 days	Melagatran 2 mg s.c. up to 30 min before surgery, then melagatran 3 mg at least 8 h after surgery, then ximelagatran 24 mg orally b.d. for 811 days versus Enoxaparin 40 mg s.c. o.d., starting 12 h before surgery for 811 days	hip or knee replacement	parallel group double-blind Europe

References

METHRO I, 2002:

Eriksson BI, Arfwidsson AC, Frison L, Eriksson UG, Bylock A, Klebo P, Fager G, Gustafsson D A dose-ranging study of the oral direct thrombin inhibitor, ximelagatran, and its subcutaneous form, melagatran, compared with dalteparin in the prophylaxis of thromboembolism after hip or knee replacement: METHRO I. MELagatran for THRombin inhibition in Orthopaedic surgery. *Thromb Haemost* 2002;87:231-7 [[11858482](#)]

METHRO II, 2002:

Eriksson BI, Bergqvist D, Klebo P, Dahl OE, Lindbratt S, Bylock A, Frison L, Eriksson UG, Welin L, Gustafsson D Ximelagatran and melagatran compared with dalteparin for prevention of venous thromboembolism after total hip or knee replacement: the METHRO II randomised trial. *Lancet* 2002;360:1441-7 [[12433510](#)]

Platinum (Colwell), 2003:

Colwell CW Jr, Berkowitz SD, Davidson BL, Lotke PA, Ginsberg JS, Lieberman JR, Neubauer J, McElhattan JL, Peters GR, Francis CW Comparison of ximelagatran, an oral direct thrombin inhibitor, with enoxaparin for the prevention of venous thromboembolism following total hip replacement. A randomized, double-blind study. *J Thromb Haemost* 2003;1:2119-30 [[14521593](#)]

METHRO III, 2002:

Eriksson BI, Agnelli G, Cohen AT, Dahl OE, Mouret P, Rosencher N, Eskilson C, Nylander I, Frison L, Ogren M Direct thrombin inhibitor melagatran followed by oral ximelagatran in comparison with enoxaparin for prevention of venous thromboembolism after total hip or knee replacement. *Thromb Haemost* 2003;89:288-96 [[12574809](#)]

Mouret P [The oral direct thrombin inhibitor Ximelagatran Prophylaxis of venous thromboembolism in hip and knee replacement] *Hamostaseologie* 2002;22:21-4 [[12215757](#)]

Eriksson BI Clinical experience of melagatran/ximelagatran in major orthopaedic surgery. *Thromb Res* 2003;109 Suppl 1:S23-9 [[12818631](#)]

Phase II (Heit), 2001:

Heit JA, Colwell CW, Francis CW, Ginsberg JS, Berkowitz SD, Whipple J, Peters G Comparison of the oral direct thrombin inhibitor ximelagatran with enoxaparin as prophylaxis against venous thromboembolism after total knee replacement: a phase 2 dose-finding study. *Arch Intern Med* 2001;161:2215-21 [[11575978](#)]

EXPRESS, 2003:

Eriksson BI, Agnelli G, Cohen AT, Dahl OE, Lassen MR, Mouret P, Rosencher N, Klebo P, Panfilov S, Eskilson C, Andersson M, Freij A The direct thrombin inhibitor melagatran followed by oral ximelagatran compared with enoxaparin for the prevention of venous thromboembolism after total hip or knee replacement: the EXPRESS study. *J Thromb Haemost* 2003;1:2490-6 [[14675083](#)]

Glynn O The express study: preliminary results. *Int J Clin Pract* 2003;57:57-9 [[12587945](#)]

2 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.