ADVANCE 2 2010

NCT00452530

1 Treatments

Studied treatment  apixaban 2.5mg twice daily during 12 days
started 12—24 h after wound closure

Control treatment  enoxaparin 40mg once daily 12 days
started 12 h before surgery

Concomittant treatments  -

Age (mean), years  67 y

Female  72%

exoxaprin regimen  started before surgery

treatment duration  12 days

BMI (kg/m²)  29.2

2 Patients

Patients  patients undergoing elective unilateral or bilateral total knee replacement

Inclusion criteria  scheduled to have unilateral elective total knee replacement or same-day
bilateral knee replacement, including revision

Exclusion criteria  active bleeding or a contraindication to anticoagulant prophylaxis, or needed
continuing anticoagulant or antiplatelet treatment; uncontrolled hypertension; active hepatobil-
ary disease; impaired renal function; thrombocytopenia, anaemia, heparin allergy; allergy to
radiographic contrast dye; other disorders preventing bilateral venography

Total hip replacement  0%

Total knee replacement  100%

Weight, kg,  78 kg

general anesthesia  35.5%

included in Jansen meta-analysis  -

History of venous thromboembolism (%)  2% (DVT)

Use of cement  91.5%
Estimated creatinine clearance >60 ml/min 83%

Previous orthopedic surgery (%) 27%

Duration of surgery (min) 94.8 min

mean follow-up 12 days

test intervalle 2-4 (3)

3 Methods

Blinding  double blind

Design  Parallel groups

Centers  125

Geographical area  27 countries

Sizes  1528/1529

4 Results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>T1</th>
<th>T0</th>
<th>d</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>myocardial infarction</td>
<td>1/1528</td>
<td>1/1529</td>
<td>1.00</td>
<td>[0.06; 16.01]</td>
</tr>
<tr>
<td>total VTE and all-cause mortality</td>
<td>147/976</td>
<td>243/997</td>
<td>0.62</td>
<td>[0.49; 0.78]</td>
</tr>
<tr>
<td>major VTE (fatal and non fatal DVT,PE)</td>
<td>13/1195</td>
<td>26/1199</td>
<td>0.50</td>
<td>[0.26; 0.98]</td>
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<tr>
<td>major bleeding</td>
<td>9/1501</td>
<td>14/1508</td>
<td>0.65</td>
<td>[0.28; 1.50]</td>
</tr>
<tr>
<td>death</td>
<td>2/1528</td>
<td>0/1529</td>
<td>5.00</td>
<td>[0.24; 104.31]</td>
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<tr>
<td>Symptomatic venous thromboembolism</td>
<td>7/1528</td>
<td>7/1529</td>
<td>1.00</td>
<td>[0.36; 2.76]</td>
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<tr>
<td>DVT (asymptomatic or symptomatic)</td>
<td>142/971</td>
<td>243/997</td>
<td>0.60</td>
<td>[0.48; 0.76]</td>
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<tr>
<td>proximal DVT</td>
<td>9/1192</td>
<td>26/1199</td>
<td>0.36</td>
<td>[0.17; 0.76]</td>
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<td>distal DVT</td>
<td>-/3054</td>
<td>-/0</td>
<td>NA</td>
<td>-</td>
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<tr>
<td>non-fatal PE</td>
<td>-/3054</td>
<td>-/0</td>
<td>NA</td>
<td>-</td>
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<tr>
<td>symptomatic DVT</td>
<td>3/1528</td>
<td>7/1529</td>
<td>0.47</td>
<td>[0.13; 1.66]</td>
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<tr>
<td>asymptomatic DVT</td>
<td>-/3054</td>
<td>-/0</td>
<td>NA</td>
<td>-</td>
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<tr>
<td>coronary events</td>
<td>1/1501</td>
<td>1/1508</td>
<td>1.00</td>
<td>[0.10; 9.67]</td>
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<td>major or clinically relevant non-major bleeding</td>
<td>53/1501</td>
<td>72/1508</td>
<td>0.74</td>
<td>[0.52; 1.06]</td>
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<tr>
<td>all bleeding</td>
<td>-/1528</td>
<td>-/1529</td>
<td>NA</td>
<td>-</td>
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5 References