Ximelagatran reduced venous thromboembolism more than warfarin after total knee replacement


Clinical impact ratings IM/Ambulatory care 的关键内部医学 重要的血液学

Q In patients having total knee replacement, is ximelagatran better than warfarin in preventing venous thromboembolism (VTE)?

CONCLUSION

In patients having total knee replacement, ximelagatran, 36 mg twice daily, was more effective than warfarin in preventing venous thromboembolism.

Abstract and commentary also appear in ACP Journal Club.

MAIN RESULTS

Fewer patients who received ximelagatran, 36 mg, had an occurrence of the composite primary endpoint than did patients who received warfarin (table). The ximelagatran 24 mg group did not differ from the warfarin group (table). Neither ximelagatran group differed from warfarin for the secondary composite endpoint of proximal DVT, PE, and all cause mortality (p values >0.10). Groups did not differ for bleeding (table).

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![Table showing outcomes and event rates](http://ebm.bmj.com/content/9/4/106/suppl/DC1.png)

**Table 1. Outcomes X dose Event rates RRR (95% CI) NNT (CI)**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>X dose</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite primary endpoint</td>
<td>36 mg</td>
<td>20.3% v 27.6% 26% (9.9 to 40)</td>
<td>14 (9 to 40)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 mg</td>
<td>24.9% v 27.6% 9.8% (–8.8 to 25)</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>36 mg</td>
<td>0.8% v 0.7% 18% (–61 to 264)</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 mg</td>
<td>0.8% v 0.7% 20% (–61 to 270)</td>
<td>Not significant</td>
<td></td>
</tr>
</tbody>
</table>

*Composite primary endpoint = venous thromboembolism, pulmonary embolism, and all cause mortality. Abbreviations defined in glossary; NNT, NNH, and CI calculated from data in article.*

**METHODS**

Design: randomised controlled trial (Exanta Used to Lessen Thrombosis A [EXULT A]).

Allocation: concealed.*

Blinding: blinded [clinicians, patients, data collectors, outcome assessors, and data analysts].*

Follow up period: 4–6 weeks.

Setting: 116 centres in the US, Canada, Israel, Mexico, and Brazil.

Patients: 2301 patients who were having primary total knee replacement and weighed between 40 and 136 kg. Exclusion criteria included pneumatic leg compression; immobilisation >3 days; major surgery, stroke, myocardial infarction, or receipt of study drug <30 days before surgery; increased risk of bleeding <90 days before surgery; increased risk of bleeding <90 days before surgery; uncontrolled hypertension; thrombocytopenia; drug or alcohol abuse in the past 6 months; and potential for pregnancy.

Intervention: twice-daily tablets of ximelagatran (Exanta, AstraZeneca), 36 mg (n = 775); 24 mg (n = 762); or once daily warfarin (Coumadin, Bristol-Myers Squibb) (n = 764). Placebos were given for each study drug. Ximelagatran was started >12 hours after surgery when haemostasis had been achieved and warfarin was started the evening of the day of surgery and adjusted to achieve an international normalised ratio (INR) of 2.5.

Outcomes: composite primary endpoint of total deep venous thrombosis (DVT), pulmonary embolism (PE), and all cause mortality during treatment (7–12 d); composite of proximal DVT, PE, and all cause mortality; and bleeding.

Patient follow up: 2285 patients (99%) (mean age 68 y, 62% women) were included in the safety analysis and 1851 (80.4%) in the efficacy analysis.

*See glossary.

†Information provided by author.