Ximelagatran prevented secondary venous thromboembolism


Clinical impact ratings GP/FP/Primary care ★★★★★★ IM/Ambulatory care ★★★★★☆ Haematology ★★★★★★

What is the long term efficacy and safety of ximelagatran after 6 months of standard anticoagulant therapy for secondary prevention of venous thromboembolism (VTE)?

METHODS

- **Randomised placebo controlled trial (Thrombin Inhibitor in Venous Thromboembolism [THRIVE III]).
- **Concealed allocation.
- **Blinded (clinicians, patients, data collectors, outcome assessors, and data analysts).
- **Follow up period: 18 months.
- **Setting: 142 centres in 18 countries.
- **Patients: 1233 patients who were >18 years of age with symptomatic, objectively confirmed deep venous thrombosis (DVT) or pulmonary embolism (PE) and had received anticoagulant therapy for 6 months with no recurrent VTE event. Exclusion criteria: indication for continuous anticoagulant therapy, haemoglobin level <9.0 g/dl, platelet count <90 000/mm3, pregnancy, lactation, expected survival <18 months, renal impairment, clinically important liver disease, or persistent elevation of the aminotransferase level >3 times the upper limit of normal.
- **Intervention: twice daily ximelagatran, 24 mg (n = 612), or placebo (n = 611) for 18 months. All patients discontinued anticoagulant therapy but did not begin study treatment until the international normalised ratio (INR) was <1.5.
- **Outcomes: VTE (recurrent DVT and PE), major and minor bleeding, and all cause mortality.
- **Patient follow up: 1223 patients (99%) (mean age 57 years, 55% men) were included in the intention to treat analysis.

MAIN RESULTS

Fewer patients who received ximelagatran had recurrent VTE events than did patients who received placebo (table). Groups did not differ for major or minor bleeding or for all cause mortality (table).

CONCLUSION

In patients with deep venous thrombosis or pulmonary embolism receiving standard anticoagulant therapy for 6 months, ximelagatran reduced recurrent venous thromboembolism and did not increase bleeding.

Abstract and commentary also appear in ACP Journal Club.

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Ximelagatran v placebo for secondary prevention of venous thromboembolism (VTE) at 18 months*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Ximelagatran</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE</td>
<td>2.8%</td>
<td>12.6%</td>
<td>83% (69 to 90)</td>
<td>10 (9 to 12)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>1.1%</td>
<td>1.4%</td>
<td>77% (143 to 72)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.1%</td>
<td>1.3%</td>
<td>16% (65 to 273)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Major and minor bleeding</td>
<td>23.9%</td>
<td>21.0%</td>
<td>16% (6 to 44)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary: RRR, RRI, NNT, NNH, and CI calculated using Cox proportional hazards ratio in article.