THERAPEUTICS

Ximelagatran was non-inferior to warfarin in preventing stroke and systemic embolism in atrial fibrillation


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

MAIN RESULTS

Analysis was by intention to treat. Ximelagatran was not inferior to warfarin for stroke and systemic embolism (table), or for the composite secondary endpoints. An on treatment analysis showed that ximelagatran had less combined major and minor bleeding than warfarin, and was not inferior to warfarin for major bleeding only (table). Serum alanine aminotransferase levels increased (3 times the upper limit of normal) more with ximelagatran than warfarin (6% vs 1%, p<0.001).

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CONCLUSION

In patients with atrial fibrillation at risk of ischaemic stroke, ximelagatran was non-inferior to warfarin in preventing stroke and systemic embolism.

Abstract and commentary also appear in ACP Journal Club.

Ximelagatran v warfarin in patients with atrial fibrillation at risk of ischaemic stroke at mean 17.4 months*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Ximelagatran</th>
<th>Warfarin</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke and systemic</td>
<td>1.6%</td>
<td>2.3%</td>
<td>0.7% (−0.1 to 1.4)</td>
</tr>
<tr>
<td>embolism†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major or minor bleeding†</td>
<td>25.8%</td>
<td>29.8%</td>
<td>4.0% (−6.9 to −1.1)</td>
</tr>
<tr>
<td>Major bleeding†</td>
<td>1.3%</td>
<td>1.8%</td>
<td>−0.5% (−1.2 to 0.2)</td>
</tr>
</tbody>
</table>

*CI defined in glossary.
†Intention to treat analysis.
‡On treatment analysis.
§Not significant.

Commentary

SPORTIF III compared ximelagatran, 36 mg twice daily, with therapeutic warfarin in patients with AF at moderate to high risk of thromboembolic outcomes. INR control in the warfarin group was similar to that in the community. The results, along with the recently reported SPORTIF V, showed that ximelagatran is at least as efficacious as warfarin and at least as safe for bleeding complications. See EBM notebook (http://ebm.bmjjournals.com/cgi/content/9/2/38). From a practical standpoint, ximelagatran is an easier drug to use than warfarin because it can be administered in a fixed dose regimen, without the need for laboratory monitoring of its anticoagulant effect to make dose adjustments, and does not appear to have drug and food related interactions that occur with warfarin. These advantages have the potential to greatly simplify the anticoagulant management of patients with AF. However, ximelagatran is potentially hepatotoxic (see table on web site). Most studies of long term ximelagatran showed almost all patients were asymptomatic and about half had complete resolution of transaminases despite continuing the drug. With few exceptions, transaminases resolved in the remaining patients after the drug was stopped. Although patients treated with ximelagatran will require hepatic monitoring in the initial 3 months of therapy, the intensity of such monitoring will probably not match that required for long term warfarin therapy.

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