Comparative effectiveness and safety of apixaban and low-molecular weight heparin among patients with venous thromboembolism and active cancer in an extended treatment setting


1 Guy’s and St Thomas’ NHS Trust Foundation Trust, Department of Hematological Medicine, London, United Kingdom of Great Britain & Northern Ireland
2 Bristol-Myers Squibb, Lawrenceville, United States of America
3 AmerisourceBergen Xcenda, Carrollton, United States of America
4 Pfizer Inc., Groton, United States of America

Funding Acknowledgements: Type of funding sources: Private company. Main funding source(s): Bristol Myers Squibb (BMS), Pfizer Inc.

Background: The 2020 European Society of Cardiology guidelines recommend extended anticoagulant (AC) treatment among patients with VTE and with progressive or persistent risk factors (such as cancer) as they are at a high risk of a recurrent VTE episode.

Purpose: The study evaluated the risk of recurrent VTE and major bleeding (MB) among patients with VTE and active cancer prescribed apixaban or LMWH (reference) for ≥3 months.

Methods: This retrospective study included patients ≥18 years with VTE who initiated apixaban or LMWH within 30 days following the first VTE event using a large administrative claims database, representing ≥140 million patients enrolled in US health plans. Data from July 1, 2016, through April 30, 2022, was used. Patients were required to have ≥3 months of continuous enrollment (CE) and ≥3 months of continuous primary AC treatment following the date of apixaban/LMWH initiation. The end of 3 months of primary treatment was designated as index date. The follow-up period was from the day after the index date until the earliest of disenrollment, discontinuation of index anticoagulant, switch to another anticoagulant, or the end of the study period. The MB and recurrent VTE outcomes were evaluated and compared in the follow-up period. Inverse-probability treatment weighting (IPTW) was used to balance the treatment cohorts on relevant demographic and clinical characteristics including VTE and cancer-related variables. Incidence rate for the outcomes were calculated per 100 person-years. Cox proportional hazard models were used to evaluate the adjusted risk of recurrent VTE and MB reported as hazard ratios (HR) along with 95% confidence interval (CI).

Results: After the eligibility criteria was met, the study included 13,527 apixaban and 2,914 LMWH treated patients with VTE and active cancer. Post IPTW, the treatment cohorts were balanced on baseline patient characteristics (Figure 1). In the follow-up period, the incidence rates (IR) per 100 person-years for recurrent VTE and MB were lower for apixaban than LMWH among patients with VTE and active cancer (Figure 2). Apixaban patients had a lower risk of recurrent VTE (HR: 0.42; 95% CI: 0.34–0.53) and MB (HR: 0.50; 95% CI: 0.41–0.61) when compared to LMWH (Figure 2).

Conclusion: In this observational cohort analysis of patients with VTE and active cancer, extended anticoagulation treatment of ≥3 months with apixaban was associated with a lower risk of recurrent VTE and MB compared with LMWH. Additional research is required to confirm these findings.
Figure 2. Incidence rates and Hazard ratios of Recurrent VTE and Major bleeding among IPTW-weighted Patients with VTE and Active Cancer prescribed Apixaban or LMWH for ≥3 months

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Treatment</th>
<th># of Patients on Treatment</th>
<th># of Events</th>
<th>Incidence Rate</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td>Apixaban</td>
<td>13,527</td>
<td>275</td>
<td>4.05</td>
<td>0.42 (0.34 - 0.51)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>LMWH (ref)</td>
<td>2,914</td>
<td>111</td>
<td>9.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>Apixaban</td>
<td>13,527</td>
<td>418</td>
<td>6.15</td>
<td>0.50 (0.41 - 0.61)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>LMWH (ref)</td>
<td>2,914</td>
<td>140</td>
<td>11.95</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key Notes: CI - Confidence Interval; LMWH - Low molecular weight heparin; ref - reference; VTE - Venous thromboembolism; #: Number

Recurrent VTE was defined by primary diagnosis in the inpatient setting as listed by ICD-10 diagnosis or procedure code after the index date.

Major bleeding was defined as the primary diagnosis as listed by ICD-10 diagnosis or procedure code after the index date and included gastrointestinal bleeding, intracranial hemorrhage, and major bleeding at other sites.

Figure 2