Increasing Utilization of Direct Oral Anticoagulants (DOACs) and Drug Interactions in People Living with HIV (PLWH) on Antiretroviral Therapy (ART): Data from the DC Cohort

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Background

• With effective ART, PLWH are living longer and may develop age-related co-morbidities.
• The CHEST guidelines recommend DOACs as first-line agents over warfarin for deep vein thromboembolism and pulmonary embolism treatment due to less bleeding and less frequent monitoring. Both warfarin and DOACs are considered Class I recommendations for atrial fibrillation.
• Five DOACs have been FDA approved: dabigatran (2010), rivaroxaban (2011), apixaban (2012), edoxaban (2015), and betrixaban (2017).
• DOAC dosing is complex and varies depending on several factors including age, indication for anticoagulation, body weight, and renal function.
• There are several additional challenges to widespread use of DOACs among PLWH receiving ART: Significant drug interaction potential with strong CYP3A4 and p-glycoprotein inhibitors including ritonavir (RTV) and cobicistat (COBI). Limited pharmacokinetic drug interaction data between DOACs and antiretrovirals.
• Use of CObI or RTV with rivaroxaban is not recommended; with apixaban, dose reduction is needed. With COBI, dabigatran dose reduction or avoidance may be necessary depending on renal function.
• Unlike warfarin, there are no well-established surrogate markers for monitoring the efficacy and/or toxicity of DOACs.

Methods

• The DC Cohort is a clinic-based, longitudinal observational cohort of PLWH established in 2011.
• The DC Cohort database was queried for participants who were prescribed oral anticoagulants (warfarin or DOACs).
• The analysis included participants from 11 outpatient sites from January 1, 2011 to March 31, 2017.

Study Objective

• To characterize evolving trends in oral anticoagulant use and the prevalence of concomitant use of DOACs with ritonavir or cobicistat boosted ART among PLWH in the Washington DC area.

Results

• Among 8,315 PLWH enrolled during the study period, there were 239 anticoagulant prescriptions (96 DOAC, 143 warfarin) for 207 persons.
• Most common indications for anticoagulation included VTE (26%), PE (20%), and atrial fibrillation (11.7%). Indication was not documented in 43.1%.

Table 2: Characteristics of Individuals Prescribed DOACs and Warfarin

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DOAC (n=96)</th>
<th>Warfarin (n=143)</th>
<th>Total (n=239)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Anticoagulation Initiation, Yrs (mean ± SD)</td>
<td>58.40 ± 9.07</td>
<td>58.13 ± 13.87</td>
<td>58.30 ± 11.06</td>
</tr>
<tr>
<td>Male (%)</td>
<td>45.8</td>
<td>52.1</td>
<td>49.8</td>
</tr>
<tr>
<td>BMI, kg/m² (mean ± SD)</td>
<td>27 ± 6</td>
<td>28 ± 8</td>
<td>27 ± 8</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>42 (44%)</td>
<td>52 (36%)</td>
<td>47 (38%)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>60 (62%)</td>
<td>75 (52%)</td>
<td>75 (31%)</td>
</tr>
<tr>
<td>Renal Impairment or dialysis (n=10)</td>
<td>9 (9.6)</td>
<td>15 (10%)</td>
<td>24 (10%)</td>
</tr>
<tr>
<td>CKD (%)</td>
<td>42 (44%)</td>
<td>54 (37%)</td>
<td>56 (24%)</td>
</tr>
</tbody>
</table>

Figure 1: Trends in Overall Oral Anticoagulant Use in the DC Cohort, 2011-2016

Figure 2: New Oral Anticoagulant Starts in the DC Cohort, 2011-2016

Conclusions

• In this cohort, DOAC use increased significantly over time from 3% of all anticoagulant prescriptions in 2011 to 43% in 2016. Rivaroxaban was the most prescribed DOAC.
• Despite the recommendation to avoid co-administration with ritonavir or cobicistat boosted ART, concomitant use was documented in 29% of rivaroxaban recipients.
• Feedback should be provided to clinicians on DOAC utilization trends and potential ART drug interactions.
• Limitations of this analysis include: Retrospective data collection with reliance on ICD 9 and 10 codes.

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