High rates of central nervous system adverse events among patients on Dolutegravir-based regimens in Uganda

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Background
• Dolutegravir (DTG) was approved as a preferred drug for first and second-line ART regimens in 2018 by WHO1
• Observational cohorts report adverse events (AE) not detected in clinical trials such as weight gain, insomnia and higher rates of drug discontinuations2,3,4
• Few observational studies from African countries
• We described & analyzed for factors associated with developing an AE on DTG

Methods
Study population and setting
• Infectious Diseases Institute (IDI), a large urban HIV Clinic in Kampala
• Retrospective study of patients initiated on, or transitioned to, a DTG-based regimen between May 2017-June 2020

Results.
Baseline Characteristics of Patients on Dolutegravir

<table>
<thead>
<tr>
<th>Characteristic (N=4560)</th>
<th>Median (IQR)/ Mean (SD)/Freq (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>2,094 (45.9)</td>
</tr>
<tr>
<td>Age at DTG, years</td>
<td>[Median (range)] 45.0 (15 – 81)</td>
</tr>
<tr>
<td>*BMI at DTG initiation</td>
<td>[Mean (SD)] 23.2 (5.3)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>125 (2.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>768 (16.8)</td>
</tr>
<tr>
<td>ART status, ART naïve</td>
<td>97 (2.1)</td>
</tr>
</tbody>
</table>

• Majority of participants were male and were treatment-experienced.

Adverse Events by Organ System

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Number of AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>320</td>
</tr>
<tr>
<td>Cardiac</td>
<td>175</td>
</tr>
<tr>
<td>Nervous</td>
<td>175</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>135</td>
</tr>
<tr>
<td>Respiratory</td>
<td>135</td>
</tr>
<tr>
<td>General</td>
<td>135</td>
</tr>
<tr>
<td>Reproductive</td>
<td>135</td>
</tr>
<tr>
<td>Visual</td>
<td>135</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>135</td>
</tr>
</tbody>
</table>

Reasons for Dolutegravir Discontinuation

• 946 (20.7%) experienced at least one AE
• Most common reason for DTG discontinuation was hyperglycemia
• Prevalence odds ratio (POR) for experiencing an AE was higher for those aged ≥ 60 yrs (adj. POR = 2.23), 40-59 yrs (adj. POR = 1.88), and 30-39 yrs (adj. POR 1.58) compared to 15-29 yrs
• Diabetes Mellitus was associated with higher POR of experiencing an AE (adj.POR = 1.65 CI: 1.04 – 2.60)
• Males were less likely to experience an AE (adj. POR = 0.73 CI: 0.64 – 0.82).

Conclusion
Many PLHIV initiating or switching to DTG experienced central nervous system AEs. Older age, being diabetic and being female were associated with higher risk of AEs. Hyperglycaemia was the commonest reason for discontinuation of therapy

References