Policy Recommendations for ART in PrEP Seroconverters

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Background

- Pretreatment drug resistance rates are increasing in low-income and middle-income countries (LMIC)
- Since 2016, WHO ART guidelines include dolutegravir (DTG)-based HIV treatment as an alternative first-line regimen
- In 2017, WHO recommended transitioning to DTG in countries where prevalence of resistance to NNRTIs efavirenz (EFV) or nevirapine (NVP) exceeds 10%
- In 2018, due to safety concerns, the WHO clarifies that DTG remains a preferred first-line ARV drug for women of childbearing potential who are using consistent and reliable contraception

Objective


CONSIDERATIONS

- Being on PrEP while having HIV (which can occur due to starting PrEP despite having HIV or due to infection while on PrEP) leaves an individual susceptible to drug resistance to NRTIs used in the PrEP regimen, such as emtricitabine (FTC), Tenofovir (TDF), and/or Lamivudine (3TC)
- When HIVDR to NRTIs develops, EFV-based first-line ART regimens may become particularly susceptible to virologic failure and NNRTI resistance emergence
- This risk is present but diminished with first-line ART regimens containing DTG or protease inhibitors (PI)

Methods

- GEMS modeled the potential impact of HIVDR among PrEP users, in the context of KwaZulu Natal (KZN) South Africa [AIDS 2018]
- To develop recommendations for policymakers as they consider timelines and priorities for first-line ART we:
  - Assessed evidence generated by modeling analyses
  - Evaluated ART and PrEP guidelines in three countries - Kenya, South Africa, and Zimbabwe, and reviewed their current recommendations for first-line ART regimens and whether recommendations existed for recent (within 3 months) PrEP users

Results

- Non-EFV options, namely DTG, are currently included as a first-line regimen choice in South Africa and Kenya, but not Zimbabwe (Table 1)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>South Africa</th>
<th>Kenya</th>
<th>Zimbabwe</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF + 3TC (or FTC) + EFV</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>TDF + 3TC + DTG</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>TDF + 3TC (or FTC) + RPV</td>
<td>X</td>
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- There are no specific ART recommendations, across all three countries, for recent PrEP users who are diagnosed with HIV
- GEMS modeling predicts that impact of PrEP is dependent on avoidance of use of EFV-based ART by people who have recently used PrEP, to avoid increases in NNRTI resistance which would undermine the effects of ART (Figure 1, based on projection of 7.6% of FSW and AGYW on PrEP over next 20 years) [AIDS 2018; Manuscript in preparation]

Policy Recommendations

- Country ART guidelines should recommend avoidance of NNRTI based first line ART regimen in PrEP users who are diagnosed with HIV (see Figure 2)
- People found to have HIV despite current or recent PrEP use should be monitored for clinical and virologic response to ART to inform future treatment recommendations for the individual, and policy recommendations for the global community

For more information about GEMS, and to view HIV drug resistance monitoring support materials, visit: www.gems.pitt.edu/toolkit