HIV Resistance Patterns in a Cohort of Adults Living with HIV Failing First-line Efavirenz-based Antiretroviral Therapy in South Africa

Authors: BE Bosch1, SM Sokhela1, JF Woods1, E Bhaskar1, K Moller1, N Manentsa1, FWD Venter1

1. Ezintsha, a sub-division of Wits Reproductive Health and HIV Institute, University of the Witwatersrand, Johannesburg, South Africa.

Background

Human immunodeficiency virus (HIV) drug resistance poses a serious threat to antiretroviral therapy (ART) regimens. The ADORE study was designed to assess the efficacy of doravirine-based ART in people living with HIV (PLWH) experiencing virological failure on efavirenz-based first-line ART in Johannesburg, South Africa. This paper reviews the resistance patterns obtained thus far, with particular reference to doravirine, in participants screened for the aforementioned study.

Method

We are in the process of conducting a single-arm, phase 3, switch study to assess the efficacy of doravirine/lamivudine/tenofovir disoproxil fumarate in PLWH experiencing virological failure on first-line efavirenz-based ART with non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance. HIV genotypic drug resistance profiles are obtained at screening visits and major drug resistance mutations (DRMs) scored using the Stanford University HIV Drug Resistance Database, with the corresponding algorithm used to predict drug susceptibility.

Results

A total of 40 individuals have been screened to date, with HIV genotypic drug resistance profiles obtained in 21 of those with unsuppressed viral loads. Of these participants, all were black, and 76.1% were female. The mean age was 35 years, and the mean baseline viral load 64 350 cp/mL with participants on ART for an average of 6 years.

At screening, major NNRTI resistance mutations associated with the highest levels of reduced susceptibility to doravirine (i.e., M230L, F227L, V106M and Y188L) were present in 57.1% (95% CI [35.9 – 78.3]) of participants, although 95.2% (95% CI [86.1 – 100.0]) exhibited varying levels of resistance to doravirine.

Conclusion

Despite a small sample size, these insights offer valuable information into the resistance patterns of PLWH in South Africa, failing NNRTI-based first-line ART regimens. Cross-resistance within NNRTIs may be more prevalent with doravirine than recorded in previous clinical trials, this potentially compromising their role as an option for patients failing efavirenz-based regimens, particularly with the introduction of dolagluriv in ART programmes in South Africa. However, the clinical significance of this genotypic resistance is still poorly understood.

References:


Table 1: Significant NNRTI Drug Resistance Mutations Per Participant

<table>
<thead>
<tr>
<th>Mutation</th>
<th>ddNRTI resistance</th>
<th>nNRTI resistance</th>
<th>PI resistance</th>
</tr>
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<tbody>
<tr>
<td>K103N</td>
<td>Low</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
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<td>Intermediate</td>
<td>High</td>
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<tr>
<td>K103E</td>
<td>Low</td>
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Corresponding Author: Bronwyn Bosch
Email: bosch@uctinteza.org
Website: www.uctinteza.org