Impact of HIV-1 Drug Resistance Testing on Clinical Outcome of Patients Receiving Highly Active Antiretroviral Therapy in Barbados

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Background

- HIV-1 drug resistance first identified in Barbados in 2005 (collaboration with Martinique and Vancouver, Canada)
- HIV-1 drug resistance testing has important role in guiding HAART in drug experienced patients failing on medication
- Role in monitoring appearance of resistant HIV strains in drug naïve patients
Objective

- To determine the impact and usefulness of HIV-1 drug resistance testing (HIVDRT) as a clinical tool for guiding treatment of HIV-1 positive patients failing HAART in Barbados.
Design and Methods

- 55 patients failing HAART (viral load >1000 copies/ml) were recruited into the study between January 2007-January 2009.
- Viral loads measured by RT-PCR
- CD4 measured by flow cytometry
- HIVDRT was carried out at the BC Center for Excellence for HIV/AIDS in Vancouver Canada.
LRU Barbados: patient failing HAART (VL >1000 copies/ml)

VIRCO: database of known mutations obtain drug resistance profile

BC Centre Canada: sequence pol, rt genes

change medication

plasma

mutations
Results

- 47/55 patients were recommended for a change in treatment regimen based on the presence of drug resistance.
- 5 patients defaulted before intervention
- 42/55 patients received a regimen change based on HIVDRT.
Results cont’d

- 8/55 patients were *not* recommended for regime change based on negative drug resistance
  - Intervention consisted of intensive adherence counseling
Successful intervention

- **76% (32/42)** of patients receiving a change in ART with 6 month follow-up experienced a successful intervention:
  - before HIV-DRT: 12900 copies/ml (CI: 12670, 101482)
  - After HIV-DRT: 40 copies/ml (CI: 36, 371)
  - (P<0.0001 Mann Whitney U Test)
Unsuccessful intervention

- **14% (6/42)** of patients did not achieve a 2-fold reduction in viral load at 6-month follow-up.
- **10% (4/42)** of patients died.
Impact of intervention on CD4 levels

Success group

Unsuccessful group
Patients not recommended for intervention

- The 8 patients not recommended for regime change
  - intervention consisted of intensive counseling
  - Before: 7120 (0, 422972)
  - After: 126 (0, 36691)
  - P=0.10, Mann-Whitney
Clinical outcomes – success group

0/40 deaths in success group and those patients not deemed candidates for regime change based on negative HIV-DRT

Good outcome linked to adherence

31/40 patients exhibited “good” adherence to medication
Unsuccessful group

**ALL** patients who died and **all** patients who were unable to control viral load failed to adhere to their new ART regimen

**10/10** patients exhibited “poor” adherence
# Resistance mutations found

<table>
<thead>
<tr>
<th>Successful Treatment Intervention</th>
<th>NRTI'S</th>
<th>NNRTI'S</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAJOR Resistance</td>
<td>25/32 - 3TC</td>
<td>25/32 - EFV/NVP</td>
<td>2/32 - IND, NFV</td>
</tr>
<tr>
<td>Reduced Response to Drug</td>
<td>21/32 - AZT, ddi, ABC</td>
<td>NONE</td>
<td>3/32 IND,NFV</td>
</tr>
<tr>
<td>Most common MUTATION</td>
<td>22/32 - 184V</td>
<td>17/32 - 103N</td>
<td></td>
</tr>
<tr>
<td><strong>Unsuccessful Intervention</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAJOR Resistance</td>
<td>4/6 - 3TC</td>
<td>6/6 - EFV/NVP</td>
<td>NONE</td>
</tr>
<tr>
<td>Reduced Response to Drug</td>
<td>4/6 - DDI/ ABC</td>
<td>NONE</td>
<td>NONE</td>
</tr>
<tr>
<td>Most common MUTATION</td>
<td>184V</td>
<td>103N</td>
<td>NONE</td>
</tr>
<tr>
<td><strong>Deceased</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAJOR Resistance</td>
<td>2/4 - 3TC</td>
<td>2/4 - EFV/NVP</td>
<td>NONE</td>
</tr>
<tr>
<td>Reduced Response to Drug</td>
<td>2/4- AZT, DDI,ABC</td>
<td>NONE</td>
<td>NONE</td>
</tr>
<tr>
<td>Most common MUTATION</td>
<td>184V</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No treatment change</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAJOR Resistance</td>
<td>1/6- 3TC/TDF</td>
<td>2/6 -EFV/NVP</td>
<td>1/6 - IND</td>
</tr>
<tr>
<td>Reduced Response to Drug</td>
<td>1/6 - DDI/ABC</td>
<td>NONE</td>
<td>1/6 - NFV, LPV/r</td>
</tr>
<tr>
<td>Most common MUTATION</td>
<td></td>
<td>103N</td>
<td></td>
</tr>
</tbody>
</table>
Resistance mutations found

Main resistance mutations found in the NNRTI class of drugs, which are used as the backbone for HAART regimens in Barbados.

High levels of mutations were also found in the NRTI class of drugs mainly to 3TC and FTC.
Conclusions

- HIV drug resistance testing has proven to be a valuable tool in reversing treatment failure on HAART with a success rate of 76%.
- Poor treatment outcomes linked to non-compliance.
- Illustrates need for multi-disciplinary team approach to support and encourage patients.
A paradox

- Developing countries employing an inexpensive NNRTI backbone have greatest need for expensive HIV-DRT intervention

- **Recommend** HIV-DRT in the Caribbean setting

- This recommendation has been acknowledged and implemented in Barbados
Contributors

- MOH - Dr. Anton Best, Dr. Dale Babb
- CDRC - Professor Clive Landis
- LRU – Professor Akin Abayomi