Integrated adherence counselling using biomedical and socio-economic information

Lucas Hermans, MD
Adherence, a daily concern...

I have 35 yr old female.
Started HAART June 2018.
CD4 02 WT 50Kg
Tolerating meds well.
Now c/o weight loss.
Gud appetite, food avails.
No other symptoms.
Got investigations cxr-Nadig radiologist report.
Hb 10.7
dl pt 764 WBC 0.66 CRP 20.
LFTs basically normal.
Creative 152.
Clinically wasted but in distress Ambulant.
What next can I do for this lady?

With a VL of 8320000
I don't believe the patient was taking treatment, patients with resistance don't have kind of VL

Ok

You
So it means that this insta.
failure is adherence related.
likely not caused by resistance.

Even the viral load of
234000 before even look at the resistance pattern
indicates that the patient has poor compliance.

What's the PI score? What
from the results, your patient doesn't have PI resistance.

I agree

Evidence of poor adherence... 😞 😞 😞
...we spent so much time educating patient...then
Insight in adherence

- Measure self-reported adherence
- Perform pill counts, review clinic attendance
- Repeat viral load
- Specialized adherence testing, drug level testing
Case #1

17 year old female

Vertical transmission, presented to clinic at 8 years old (ART naïve), CD4 20 cells/mL, mother passed away shortly after birth, father taking care of his child alone.

Initiated ART: AZT/3TC/NVP. Viral rebound after 24 months of ART. Switched to 2\textsuperscript{nd} line ART (AZT/3TC/LPVR) at 10 years old.

Virological suppression on 2\textsuperscript{nd} line until 16 years old, then intermittently defaults treatment. Visits clinic irregularly.

Brought to clinic by father, who is now extremely worried:
• Virological failure for one year: last VL 57540 copies/mL
• 26 weeks pregnant
Case #1 (ctd)

- Drug resistance testing was urgently requested (t=0)
  - Intensified adherence support while awaiting test results
  - Results (now 29 weeks pregnant): **No resistance, wild-type virus**
  - VL repeated (32 weeks pregnant): <50 copies/mL

- Delivered healthy HIV-negative boy

**Retrospective drug level test during failure: NEGATIVE**
Case #2

46 year old male

Initiated on ART 38 years old, transferred in with 1\textsuperscript{st} line failure after 24 months of ART (3TC/AZT/EFV).

Switched to 2\textsuperscript{nd} line (3TC/AZT/LPVr), but never suppressed. Viral loads:

\begin{verbatim}
m6 44309 c/mL
m12 6790 c/mL
m24 4798 c/mL
m36 3981 c/mL
m48 44136 c/mL
\end{verbatim}
Case #2 (ctd)

- Drug resistance testing requested

- Third-line ART requested from third-line committee.
  - Patient switched to third-line ART and currently suppressing

Retrospective drug level test at time of failure: POSITIVE
Significance of a negative drug level test

L Hermans et al, Abstract #98, SA HIV Clin Soc
Evaluation of ITREMA strategy

First-line ART

Prospective evaluation
(ITREMA Open-label RCT)

Second-line ART

Retrospective evaluation
(Single centre clinic-based)

Retrospective evaluation
(Multicentre lab-based)
Pilot study

• Clinical implementation project
  • Adults on second-line ART at Ndlovu Medical Centre (Limpopo, SA)
  • Confirmed VL >1000 copies/mL >12 months of second-line ART

• DBS-based population-based sequencing of PR-RT at WHO reference laboratory (UMCU)
  • Drug susceptibility interpreted according to Stanford

• DBS-based LPV drug testing (UMCU)
  • DBS-based liquid chromatography-tandem mass spectrometry
  • ≥ 0.25 mg/L → “positive” result
  • Batch-wise retrospective

L Hermans, IDRW, 2017
## Pilot study - patients

### Characteristics of patients ($n = 60$)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% female</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>56.7%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>median [IQR]</td>
</tr>
<tr>
<td>Duration of ART</td>
<td></td>
<td>36.6 years [31.7 - 46.4]</td>
</tr>
<tr>
<td>Duration of second-line ART</td>
<td></td>
<td>5.0 years [2.7 - 6.2]</td>
</tr>
<tr>
<td>Duration of second-line ART</td>
<td></td>
<td>2.4 years [1.2 - 4.1]</td>
</tr>
<tr>
<td>CD4 count at start ART</td>
<td></td>
<td>98 cells/uL [47 - 1912]</td>
</tr>
<tr>
<td>CD4 count at second-line failure</td>
<td></td>
<td>226 cells/uL [104 - 357]</td>
</tr>
<tr>
<td>log HIV-RNA at 2nd line failure</td>
<td></td>
<td>4.6 log copies/ml [3.9 - 5.2]</td>
</tr>
<tr>
<td>Current ART treatment</td>
<td></td>
<td>60/60 (100%)</td>
</tr>
<tr>
<td>3TC/AZT (%)</td>
<td></td>
<td>41/60 (68.3%)</td>
</tr>
<tr>
<td>FTC/TDF (%)</td>
<td></td>
<td>10/60 (16.7%)</td>
</tr>
<tr>
<td>other (%)</td>
<td></td>
<td>9/60 (15%)</td>
</tr>
</tbody>
</table>

**Note:** ART = Antiretroviral therapy; CD4 count = CD4+ T-lymphocyte count; cells/uL = cells per microliter; IQR = Interquartile range
Pilot study – Drug resistance

- **34/59 (57.6%)** harbored DRMs to NRTI backbone
- **8/59 (13.6%)** harbored DRMs conferring major PI resistance
Pilot study – Drug level testing

65.3% of patients had a negative LPV level

Negative LPV level $\rightarrow$ 0.0% chance of PI-resistance

Positive LPV level $\rightarrow$ 35.3% chance of PI-resistance

Sens: 100% [54% - 100%]
NPV: 100% [89% - 100%]
Spec: 76% [60% - 88%]
PPV: 38% [15% - 65%]

<table>
<thead>
<tr>
<th>N = 49</th>
<th>LPV-resistance PRESENT</th>
<th>LPV-resistance ABSENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPV drug test POSITIVE</td>
<td>6 (12.2%)</td>
<td>11 (22.5%)</td>
</tr>
<tr>
<td>LPV drug test NEGATIVE</td>
<td>0 (0%)</td>
<td>32 (65.3%)</td>
</tr>
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L Hermans, IDRW, 2017
Implementation study
*(preliminary results)*

• What would be the effect of broad implementation of drug level testing?

• Collaboration with NHLS HIV genotyping lab JHB
  • Random representative sample of resistance testing requests in 2017 (Gauteng, NW, Limpopo, Mpumalanga)

• 500 unique patient samples selected
  • Adult patients
  • On LPV/r-based second-line ART
  • Last VL >1000 c/mL

• Drug level testing: batch-wise retrospective LCMS on plasma
Drug resistance 
(preliminary results)
Drug level testing
(preliminary results)

47.3% of patients had a negative LPV level

Negative LPV level → 5.9% chance of PI-resistance
Positive LPV level → 45.4% chance of PI-resistance


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<tr>
<td>LPV drug test POSITIVE</td>
<td>23.9% (119)</td>
<td>28.8% (143)</td>
</tr>
<tr>
<td>LPV drug test NEGATIVE</td>
<td><strong>2.8% (14)</strong></td>
<td>44.5% (221)</td>
</tr>
<tr>
<td></td>
<td>26.8% (133)</td>
<td>73.2% (364)</td>
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Conclusions

• Non-adherence is a major concern in HIV treatment

• The ITREMA strategy uses qualitative drug level testing to gain insight into adherence

• In second-line ART the ITREMA strategy has the potential to prevent unnecessary costly resistance testing
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