Understanding virological failure

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Virological suppression of individuals in care in South-Africa

Hermans et al. CROI 2018
Current recommendations for management of viral rebound for LMIC

1. Start ART
2. Viral load monitoring
   - VL <1000 c/mL
   - VL >1000 c/mL
     - Intensified adherence counselling
     - Repeat VL
       - VL <1000 c/mL
       - VL >1000 c/mL
         - Switch

Monitoring schedule:
- 6 and 12 months, then annually
- 3-6 months after rebound
Management of viral rebound in clinical practice

• Management according to the guidelines

Clinical follow-up of viral rebound: Observed versus recommended practice
Management of viral rebound in clinical practice

• Observed clinical practice is not as per guidelines
Management of viral rebound in clinical practice

• Observed clinical practice is not as per guidelines
• VL is measured repeatedly despite > 1000 cp result
• Switch is often postponed or not performed at all

Clinical follow-up of viral rebound: Observed versus recommended practice

- Viral load: recommended practice (WHO guidelines)
- Viral load: observed practice
- Window for transmission: recommended practice
- Window for transmission: observed practice

Hermans et al. CROI 2018
Why not to switch:

• No clinical urge, patient’s preference

• Suspected non-adherence

• Evidence of non-adherence despite intervention
  • Patient-reported/Poor clinic attendance/defaulting

➢ In case of non-adherence, low or no risk of resistance

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Year</th>
<th>Setting</th>
<th>% without resistance</th>
<th>n=</th>
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<td>Kantor</td>
<td>AIDS Res Hum Retrov</td>
<td>2002</td>
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<td>Murphy</td>
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<td>Van Zyl</td>
<td>J Med Virol</td>
<td>2011</td>
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<td>Manasa</td>
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<td>14%</td>
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Why not to switch (contin.)

• Increased drug costs

• A more complex and more toxic regimen for a patient who already struggles with one pill a day

• Patients with no resistance at first-line failure more likely to fail second-line: non-medical barriers should be explored.
Why to switch promptly

• Prolonged virological failure may lead to CD4-count decline and clinical deterioration\(^1,2\)
• Increases risk of transmission of HIV
• May allow for accumulation of resistance\(^3,4\)

2: Keiser O, Trop Med Int Health, 2010
3: Barth et al, 2012
4: Aitken et al, 2013
Viral rebound results in HCW dilemma: “To switch or not to switch?”

Switch
• Best option if resistance is present
• Unnecessary if resistance is absent

No switch
• One pill per day
• Limited toxicity
• Accumulation of resistance if present
Insight in failure

• Rapid decision-making requires additional insight into adherence and resistance

• Resistance testing is costly and complex
  • Results are frequently unreliable if a patient non-adherent
So..

Diagnostic tools to establish the cause of viral rebound are urgently required to perform targeted adherence interventions and informed timely switches to second-line ART
Evaluation of an intensified treatment monitoring strategy to prevent accumulation of HIV-1 drug resistance in resource limited settings
The ITREMA strategy

Drug level informed adherence counselling
Actively exploring non medical issues as well

Point-of-care drug level assessment

Resistance testing

New ART
Evaluation of the 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)
Prospective assessment during 1\textsuperscript{st} line ART

• ITREMA open-label RCT (NCT03357588)
  • Adult HIV-1 infected patients either initiating first-line ART or stable on first-line ART (last viral load <1000 c/mL)
  • Control arm: Monitoring according to SA/WHO guidelines
  • Intervention arm: ITREMA intensified monitoring strategy

• Implemented as pragmatic RCT at a rural clinical site (Ndlovu Care Group, Limpopo, South Africa)
  • 501 participants included, follow-up ends Q1 2019
Preliminary results of the ITREMA trial (1st line ART)

Preliminary trial results presented this week

- Pretreatment dual class drug resistance, increases risk of poor treatment outcomes (Abstract #2, IDRW)
- Predictive value of pill counts for treatment outcomes is poor, but baseline psychosocial factors do predict outcomes (Abstract #97, SA HIV Clin Soc)
- Qualitative drug level testing for LPV/EFV/DTG can be implemented and reliably performed in a resource-limited setting as a point-of-care test (Abstract #98, SA HIV Clin Soc)
Conclusions

• On-treatment virological suppression rates in SA are high

• Clinical response to viral rebound and switch to second-line ART is delayed

• The ITREMA project is an integrated platform
  • to gain insight in reasons for treatment failure
  • to evaluate the use of tools to empower healthcare workers and patients
www.itrema.org

Aiming to improve the effectiveness of HIV treatment

- Low level viremia ≠ treatment success
- Delayed response to viral rebound puts individuals and society at risk
- Use tools to generate insight in virological failure
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