Managing virological failure in people living with HIV: giving the patient a chance, not the first line!

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In order to reach the final 90 of the 90-90-90 UNAIDS goal, access to viral load (VL) monitoring must be expanded to all the people living with HIV on antiretroviral therapy.

In case of virological failure (>1000 cp/mL), WHO and national programs recommended the use of VL algorithm because of the high cost and low availability of genotyping.

Adherence counselling result in re-suppression in 46.1% (CI\textsubscript{95%} 42.6% to 49.5%) of patients, avoiding unnecessary drug regimen changes. (Meta analysis, 6280 patients, 21 studies, Ford et al. J AIDS 2019)
Among patients in first-line ART with confirmed virological failure, only 53.4% (CI 95% 40.1% - 66.8%) are appropriately switched to a different regimen. (Meta analysis, 6280 patients, 21 studies, Ford et al. J AIDS 2019)

Analyses to identify gaps and focus quality improvement to ensure that action is taken on the results of viral load testing

In the real life, management of virological cascade is a challenge

VL monitoring cascade in rural Lesotho. Glass et al. Plos One 2019
HIV viral load failure cascade, OPP-ERA project 2014-2019, 26268 patients with first VL>1000 cp/mL

**HIV virological failure cascade, by countries**

- **Burundi**: No. of pts with VL>1000 cp/mL - 4347, No. of pts with VL control within 3-6 months - 722, No. of pts switch to 2nd line ART - 58
- **Guinea**: No. of pts with VL>1000 cp/mL - 4637, No. of pts with VL control within 3-6 months - 371, No. of pts switch to 2nd line ART - 60
- **Cameroon**: No. of pts with VL>1000 cp/mL - 5718, No. of pts with VL control within 3-6 months - 384, No. of pts switch to 2nd line ART - 36
- **Cote d'Ivoire**: No. of pts with VL>1000 cp/mL - 11566, No. of pts with VL control within 3-6 months - 1547, No. of pts switch to 2nd line ART - 201

**HIV virological failure cascade, global**

- VL>1000 cp/mL: 100%
- VL control within 3-6 months: 11.7%
- 2nd line ART: 23%

See Poster WEPEB081
Objective and Methods

- Objective: to investigate reasons associated to the low use in 2\textsuperscript{nd} line ART by ART prescribers.

- Methods: quantitative and qualitative survey, during April and June 2019 in Burundi, Guinea, Cameroon and Cote d’Ivoire.

- Participants: ART prescribers and HIV program manager
  - Self administered questionnaires to ART prescribers:
    - Knowledge survey (n=71)
    - Raison associated with low 2\textsuperscript{nde} line use survey  (n=56)
  - Qualitative data: focus groups and clinical training.
## Participants characteristics

<table>
<thead>
<tr>
<th>Participants characteristics</th>
<th>knowledge survey</th>
<th>low use of 2nd line survey</th>
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<tbody>
<tr>
<td>Number</td>
<td>71</td>
<td>56</td>
</tr>
<tr>
<td>Sex ratio F/H</td>
<td>31/40</td>
<td>25/31</td>
</tr>
<tr>
<td>Age (EIQ)</td>
<td>36.5 (31-44)</td>
<td>37 (31.5-47)</td>
</tr>
<tr>
<td>Years HIV care (EIQ)</td>
<td>6 (3-9)</td>
<td>6 (3-10.75)</td>
</tr>
<tr>
<td>Medical diploma</td>
<td>62 (87%)</td>
<td>50 (89%)</td>
</tr>
<tr>
<td>Working in associative health facility</td>
<td>17 (24%)</td>
<td>13 (23%)</td>
</tr>
<tr>
<td>Country</td>
<td>Guinea: 21</td>
<td>Guinea: 18</td>
</tr>
<tr>
<td></td>
<td>Cameroon: 15</td>
<td>Cameroon: 15</td>
</tr>
<tr>
<td></td>
<td>Cote d’Ivoire: 12</td>
<td>Cote d’Ivoire: 12</td>
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<tr>
<td></td>
<td>Burundi: 23</td>
<td>Burundi: 12</td>
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ART prescribers' knowledge of VL and viral failure management

- Knowledge of the differences between CD4 and VL
- Knowledge of 2nd line treatment regimens
- Knowledge of prescription of 2nd line treatments
- Ability to interpret the VL algorithm (compliance with the 1000 cp/mL threshold)
- Ability to interpret the VL algorithm (interpretation of the delay of the control VL)

Viral load knowledge and ability to interpret VL algorithm

P<0.001
ART prescribers' point of view on the reasons associated with the low switch to 2\textsuperscript{nd} line

(\% of participants who strongly agree or somewhat agree with the proposal)

**Individual reasons**
- low involvement of prescribers in adherence intervention
- too much responsibility for prescribers
- difficulty explaining VL results to patients
- poor knowledge of the interpretation of VL results
- poor knowledge of the VL algorithm

**Organisational reasons**
- low availability of 3\textsuperscript{rd} line
- increased workload
- low availability of staff dedicated to adherence intervention
- too long delay in delivering VL results
- VL results not available in medical records

**Institutional reasons**
- fear of shortage of 2\textsuperscript{nd} line
But what happens in an almost “perfect world”?  
Retrospective survey on 29 patients in virological failure, ANSS, Burundi

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>data</th>
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<tbody>
<tr>
<td>Total number of VL measure from the initiation of ART, median (EIQ)</td>
<td>5 (3.5-6)</td>
</tr>
<tr>
<td>Turn around time VL results (days), median (EIQ)</td>
<td>12 (7-17)</td>
</tr>
<tr>
<td>Result of VL &gt;1000 cp/mL notified in the medical chart, N(%)</td>
<td>80/99 (81%)</td>
</tr>
<tr>
<td>Adherence intervention notified in the medical chart, N(%)</td>
<td>66/99 (67%)</td>
</tr>
<tr>
<td>Proportion of patients who have benefited from switch to 2nd line (%)</td>
<td>11/29 (38%)</td>
</tr>
<tr>
<td>Duration of viral replication (nb of days after the 1st VL&gt;1000 cp/mL to date of switch or date of medical chart evaluation), median (EIQ)</td>
<td>499 (400-537)</td>
</tr>
</tbody>
</table>

Median VL value at time of virological failure is associated with 2nd line switch

P=0.04

See Poster WEPEB082
The second line is seen as a rare and precious resource:

- HIV program managers:
  - Difficulties of financial prioritization: cost of second-line treatment in a context of treat all recommendations and decrease in international funding
  - Consequence: limit and control the use of the 2nd line
    "Give the first line a chance"; "we took away the second line because they were doing anything"

- ART prescribers:
  "we were told to be careful", "we must preserve the first line"; "we must be able to justify”.

Negative representation of 2nd line
  "sanction", "failure", "fear", "responsibility", "workload”.

Negative representation of patients in virological failure
  "not serious", "liars", "delinquents", "offenders”
The challenge of adherence counselling

- Adherence improvement before initiating 2\textsuperscript{nd} line is a major concern

  "you have to ensure proper adherence before moving to the 2\textsuperscript{nd} line".

However:

1) Adherence counselling and failure announcement seems mainly injunctive and dramatic

  "you have to make an effort", "you have to take your treatment regularly", "otherwise the virus will multiply", "you will get sick"

  "if he doesn't understand, you have to be hard, to scare him", “this is your last chance, after it’s death”

2) The mechanisms of virological failure are poorly analyzed.

VF is only perceived as the consequence of non adherence which is perceived as patients’ fault.

The main causes of VF spontaneously mentioned are:

- Lying and not understanding patients

  "patients lie", “if the patient tells you that he is not taking his treatment once, you can multiply by 10”

- Mains other reasons: psycho-social difficulties, unprotected sex, traditional medicine

3) Evaluation of adherence is difficult

- Undetectable VL seems often used as a proxy of adherence
The interpretation of the VL algorithm

Viral load $>1000$ copies/ml

The threshold of 1000 cp/mL is known but it’s interpretation is a challenge:

- a decrease reflects the effectiveness of adherence counselling
  "it's going down, that's good, that means we have to continue to strengthen adherence."
- an increase reflects continued non-adherence
  "not serious patient"

Repeat viral load testing after 3–6 months

- The 3-6 months period is known but it’s interpretation is a challenge:
  "if my patient had a sample in January and I had the result in March, from when I count 3 months?"

- This deadline is difficult to reach in practice:
  - VL turn around time (lab and clinical site)
  - Wait until next patients’ visit
  - Delay for re-sampling
- results returned after 6 months are considered not to comply with the algorithm

Most often, lead to further adherence intervention and new VL test
Towards an unofficial VL algorithm...?

VL > 1000 cp/mL
Evaluate for adherence concerns.
VL control 3 to 6 months later

VL <1000 cp/mL
success
1st line ART

VL >1000 cp/mL
failure
2nd line ART

VL control > 6 months

VL decrease but >1000 cp/mL
Success: continue adherence counselling
Stability or increase in VL
Failure: intensified adherence counselling

Give the 1st line ART a chance
CONCLUSIONS

• Limits: methods (no individual ITW, no ethnographic survey...), restricted to ART prescribers.

• Prescribers highlight structural and organizational reasons:
  • VL turn around time
  • Human resources concerns (HR turn-over, task delegation, workload...)
  • 2\textsuperscript{nd} (and 3\textsuperscript{rd} line) supply

• Fear of national program manager for unjustified use of 2\textsuperscript{nd} line is a limiting factor.
  • Improve 2\textsuperscript{nd} line quantification and communication between actors.

• Prescribers have a good theoretical knowledge of the VL algorithm in contrast to difficulties of interpretation and practical application.
  • VL algorithms need to be explained (or modified) to make them applicable on the field.

• Prescribers (and patients) are not prepared for failure, the announcement is most often dramatic and guilt-ridden.

• Adherence counselling is a challenge especially when patients are suffering from negative representation.
  • the mechanisms of failure are poorly analysed and patients are not prepared for 2\textsuperscript{nd} line
Recommendations: some tools developed in the frame work of the OPPERA project

• Guide: the announcement of virological failure and patient support (“let’s talk about failure” working group)
• Practical training module
• Many other tools available (english and french)

OPP-ERA toolkit link: https://toolkit-chargevirale-oppera.solthis.org
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