PAEDIATRIC HIV TREATMENT FAILURE:

CONTRASTING RESULTS BETWEEN CHILDREN AND ADOLESCENTS IN A DEDICATED PROGRAMME TO ADDRESS HIGH VIRAL LOADS IN KHAYELITSHA, SOUTH AFRICA

Jonathan Bernheimer, MD, MSc, DTM+H
Paediatrician
MSF Khayelitsha / SAMU
Background

- High treatment failure rates are seen in children and adolescents in South Africa (40% 0-14 year olds)\(^1\)

- Since 2013, Medecins Sans Frontieres (MSF) has run a programme to address high viral loads (VLs) in Khayelitsha, South Africa

- Failing patients 0-19 years old enrolled

- Intervention includes:
  - Clinical Care
  - Adherence support: (individual counseling, support groups)
  - Genotyping
  - Regimen changes when indicated

---

1. The continuum of HIV care in South Africa: implications for achieving the second and UNAIDS 90-90-90 targets Simbarashe Takuva Alison E. Brown, Yogan Pillay, Valerie Delpech and Adrian J. Puren AIDS 2017, Vol 31 No 4
Series of visits:
(Bi-weekly, then monthly)

3 months adherence then VL

Two consecutive suppressed VLs needed to be discharged
Results: Achieving VL suppression once by age

174 Total Patients 0-19 years of age
(166 total patients with at least one viral load + 8 patients LTFU before VL 1)

141/174 (81%) achieved VL suppression at least once during intervention

0-10 year olds
74/83 (89%) achieved VL suppression at least once during intervention

10-19 year olds
67/91 (74%) achieved VL suppression at least once during intervention
Results:
Achieving VL suppression two consecutive times by age

0-19 year olds
102/156 (65%) achieved VL suppression two consecutive times

0-10 year olds
56/76 (74%) VL suppression two consecutive times

10-19 year olds
46/80 (58%) achieved VL suppression two consecutive times
Results: VL Rebound

25/141 (18%) Overall Rebound Rate

0-10 year olds

10/74 (14%) experienced VL rebound

10-19 year olds

15/67 (22%) experienced VL rebound
Enrolled on a PI regimen

- Suppressed once: 92
- 22 not suppressed: TFO: 5, LTF: 6, RIC: 9
- No VLs: 2
- 2 consecutive suppressed VLs: 67
- No more VLs: TFO: 4, LTF: 1, RIC: 9
- VL rebound: 11
- 5 re-suppressed

- Fam club: 1
- RIC: 3

- TFO: 8
- LTF: 1
- Fam club: 41
- RIC: 17

87% of those enrolling, excluding the TFOs and those with no VLs yet

70% of those enrolling, excluding TFOs and those with no additional VLs

87% of those enrolling, excluding the TFOs and those with no VLs yet

70% of those enrolling, excluding TFOs and those with no additional VLs

5 re-suppressed

Fam club: 2
RIC: 3
Results: Enrolled on an NNRTI regimen

20% of those enrolled on an NNRTI, excluding the TFOs, and RIC with no VL

Enrolled on an NNRTI 62

Switched to PI

6 RIC

Suppressed Once on NNRTI 11

2 LTF
3 RIC

2 consecutive suppressed VLs:
7
Rebound: 1
(TFO)

RIC: 1
Family clubs: 5

Suppressed once 32

Unsuppressed
1 LTF
1 TFO
5 RIC

RIC: 4
Family clubs: 18
TFO: 1

84% of those switched, excluding the TFOs

No second suppressed VL:
4 fam club
3 TFO
2 RIC
Results: Suppression and rebound by regimen and age

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Suppressed 1</th>
<th>Suppressed 2</th>
<th>Rebound</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enrolled on PI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-10 years</td>
<td>63 (91%)</td>
<td>48 (76%)</td>
<td>9 (14%)</td>
</tr>
<tr>
<td>10-19 years</td>
<td>29 (74%)</td>
<td>19 (56%)</td>
<td>8 (28%)</td>
</tr>
<tr>
<td><strong>Enrolled on NNRTI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-10 years</td>
<td>3 (27%)</td>
<td>2 (20%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>10-19 years</td>
<td>8 (17%)</td>
<td>5 (12%)</td>
<td>2 (11%)</td>
</tr>
</tbody>
</table>
Results: Time to suppression by regimen

<table>
<thead>
<tr>
<th></th>
<th>Baseline regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PI</td>
</tr>
<tr>
<td>Time to 1(^{st}) suppression</td>
<td>3.9</td>
</tr>
<tr>
<td>(median time in months)</td>
<td></td>
</tr>
<tr>
<td>Time to 2(^{nd}) suppression</td>
<td>7.37</td>
</tr>
<tr>
<td>(median time in months)</td>
<td></td>
</tr>
<tr>
<td>Time to rebound after 1(^{st})</td>
<td>4.5</td>
</tr>
<tr>
<td>suppression</td>
<td></td>
</tr>
<tr>
<td>(median time in months)</td>
<td></td>
</tr>
</tbody>
</table>
Resistance

• **100% (24/24)** patients genotyped while on a NNRTI while on showed resistance

• Only 12 patients on a PI were selected to have a genotype, of which 5 were resistant (41%)

• Only **4%** of patients enrolled on a PI were found to have PI resistance
Discussion:

- High rates of VL suppression were achieved in patients enrolled on a PI and in those enrolled on a NNRTI who were switched to a PI.

- Achieving durable suppression more difficult, especially among older children.

- All patients on NNRTI regimens who did not suppress who were genotyped showed resistance.

- PI resistance is low (most patients did not require genotyping).

- Patients 10-19 years old experienced VL rebound at a higher rate than younger patients.

- Time to suppress once and twice was short, as was the time to rebounding.
Conclusions:

• High VL suppression rates are possible for patients on a PI regimen through addressing adherence barriers in a thorough manner.

• Continued monitoring and support is needed to achieve long term suppression and to avoid rebound, especially in adolescents.

• The vast majority of patients failing an NNRTI regimen will require switching to PI regimens.

• Viral suppression can be achieved in a short period of time (within 6 months) for most patients.
Thanks!

Questions?
### Results: Age by baseline regimen

<table>
<thead>
<tr>
<th>agegroup</th>
<th>PI didn’t switch</th>
<th>PI Switched</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5 y/o</td>
<td>45 (98%)</td>
<td>1 (2%)</td>
<td>46</td>
</tr>
<tr>
<td>5-10 y/o</td>
<td>28 (74%)</td>
<td>5 (13%)</td>
<td>38</td>
</tr>
<tr>
<td>10-15 y/o</td>
<td>31 (45%)</td>
<td>26 (38%)</td>
<td>69</td>
</tr>
<tr>
<td>15+ y/o</td>
<td>10 (43%)</td>
<td>7 (30%)</td>
<td>23</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>114 (65%)</strong></td>
<td><strong>39 (22%)</strong></td>
<td><strong>176</strong></td>
</tr>
</tbody>
</table>
Not sure overall about putting in this slide. Not really sure what it shows....

Is it correct that 24 patients enrolled on a NNRTI did not switch to a PI? I thought it was most of them....

MSFUser, 11/06/2017

this was in response to the request to break down by age. I mentioned in email - the numbers get small and it will be way too complicated.

Maybe you can move it to the end as an extra slide and if people ask if there was a difference between PI and NNRTI by age, you can show?

re switches: this includes those 12 that were LTF, no VL yet, etc.

PS I corrected this slide - there was one unswitched that I moved to switch. Need to check - inconsistent PI NNRTI data for him

MSFUser, 11/06/2017
## Results: PI versus NNRTI regimen

<table>
<thead>
<tr>
<th>Patients enrolled on a PI</th>
<th>Patients enrolled on a NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>92/105 (88%) suppressed once</td>
<td>11/23 (48%) suppressed once</td>
</tr>
<tr>
<td>2 consecutive suppressed VLs: 67/93 (72%)</td>
<td>Reained on NNRTI</td>
</tr>
<tr>
<td>VL rebound: 17/92 (18%)</td>
<td>Switched to PI</td>
</tr>
<tr>
<td></td>
<td>32/39 (82%) suppressed once</td>
</tr>
<tr>
<td></td>
<td>2 consecutive suppressed VLs: 7/12 (58%)</td>
</tr>
<tr>
<td></td>
<td>VL rebound: 2/11 (18%)</td>
</tr>
<tr>
<td></td>
<td>2 consecutive suppressed VLs: 23/34 (68%)</td>
</tr>
<tr>
<td></td>
<td>VL rebound: 4/32 (13%)</td>
</tr>
</tbody>
</table>
I think since we have the next 2 slides that I will remove this one. I don't think I will have the time to talk about all of it.

MSFUser, 11/06/2017

Ya I agree - made the other two slides as alternatives. We should chat about cutting down on the content of next 2 slides too - probably too much detail, but I wanted you to see all data before deciding what to cut.

MSFUser, 11/06/2017
Results: Outcomes by regimen

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>PI</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>median days</td>
</tr>
<tr>
<td>Family Club</td>
<td>45</td>
<td>378 (322-490)</td>
</tr>
<tr>
<td>RIC</td>
<td>43</td>
<td>499 (110-870)</td>
</tr>
<tr>
<td>LTF</td>
<td>8</td>
<td>427 (304-582)</td>
</tr>
<tr>
<td>TFO</td>
<td>18</td>
<td>296 (133-420)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>113</td>
<td>387 (252-567)</td>
</tr>
</tbody>
</table>

87% of those leaving the program, excluding TFOs were transferred to FC

82% of those leaving the program, excluding TFOs were transferred to FC
Not entirely sure I understand this - For PIs it looks like 45 patients were transferred to a family club. It doesn't seem like this is 87% even with excluding LFT/TFO.
Same with the 82% - not understanding these numbers...

MSFUser, 11/06/2017

See notes and see if you agree with how i worked it out. My feeling is that we shouldn't include the RIC (hence 'completed the program - which i changed to 'leaving the program) because they haven't had a chance to complete the program yet, but we should probably note that there are some children that have been in the program for a long time, which is also probably an unfavorable outcome.

(note the animations - you might want to change the order of how things appear etc.)

MSFUser, 11/06/2017
CD4 counts among rebounds

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>mean</th>
<th>median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline CD4</td>
<td>25</td>
<td>759.96</td>
<td>617</td>
<td>617(442-1159)</td>
</tr>
<tr>
<td>Last CD4 before rebound</td>
<td>21</td>
<td>887</td>
<td>643</td>
<td>643(534-1011)</td>
</tr>
</tbody>
</table>
Why 25 at baseline and only 21 at the last CD4 before rebound?

May not show this slide - time will be short I think.....

missing data. Can look up on NHLS for those 4 if you want. Let me kow if you want to keep this.