Favorable outcomes of pediatric second-line protease inhibitor-based antiretroviral treatment in Uganda

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Coverage of antiretroviral treatment in children

Pediatric HIV treatment: the public health approach

First-line treatment: NNRTI*  
97%

Second-line treatment: PI  
3%

* Children >3 years
Objectives

- Assess the treatment outcomes of children on second-line ART
- Determine risk factors for second-line treatment failure
- Evaluate patterns of HIV drug resistance in children failing second-line ART
MARCH Uganda

- Prospective observational cohort study

- Inclusion criteria second-line cohort:
  - Children ≤ 12 years of age
  - Failing first-line treatment

- 24 months follow-up

- Viral load and HIV drug resistance testing at treatment initiation and every 6 months (retrospective)

- Treatment failure: 2 consecutive VL >1000 cps/ml or death
Study flow

Enrolled in MARCH at first-line ART initiation
- N=14

Enrolled in MARCH at first-line ART failure
- N=50

MARCH second-line cohort
- N=64

Treatment failure
Second-line cohort

- Median age: 5.7 years
- WHO stage III or IV: 45%
- First-line regimen: NNRTI-based (92%), 3NRTI (8%)
- Second-line regimen: LPV/r-based (100%)
Follow-up

MARCH second-line cohort
24-month follow-up

Start second-line ART
N=64

Lost to follow-up
N=4

Treatment success
N=48

Treatment failure
N=12
Treatment failure

- Treatment failure: 12/64 (18.8%)
  - Died: 2 (3.1%)
  - Viral load >1000 cps/ml: 10 (15.6%)

- Treatment failure associated with:
  - Underweight: 33% vs 13%, p=0.04
  - Suboptimal adherence: 75% vs 33%, p=0.02

- Not associated with NRTI resistance at 2\textsuperscript{nd} line ART initiation
HIV drug resistance

![Graph showing percentages of children with mutations for NNRTI, NRTI, and PI categories. The graph indicates higher resistance percentages for second-line failure compared to second-line initiation for NNRTI and NRTI categories.]
Conclusions: Treatment failure

- 18.8% treatment failure after 24 months

- Children:
  - 32.1%: MARCH 1\textsuperscript{st} line
  - 16-40%: 2\textsuperscript{nd} line South-Africa, Uganda, Kenya, Thailand

- Adults:
  - 23.1%: meta-analysis LMIC

References:
- Ajose et al. AIDS 2012; 26 (8)
Conclusions: HIV drug resistance

• NRTI resistance at second-line initiation no risk factor for treatment failure

• Other studies on PI resistance at failure:
  • Thailand: 11%
  • Botswana: 25%
  • South-Africa: 49%

Conclusions and recommendations

- PI-based treatment
- Long-term follow-up data
- Adherence support
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## Pediatric ART guidelines

<table>
<thead>
<tr>
<th>WHO guideline</th>
<th>Age group</th>
<th>PMTCT exposure</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; line</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; line</th>
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<tbody>
<tr>
<td>2010</td>
<td>&lt;2 years</td>
<td>Exposed</td>
<td>PI+ 2NRTI</td>
<td>NNRTI+ 2NRTI</td>
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<tr>
<td></td>
<td></td>
<td>Unexposed</td>
<td>NNRTI+2 NRTI</td>
<td>PI+2NRTI</td>
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<tr>
<td></td>
<td>≥2 years</td>
<td>Any</td>
<td>NNRTI+2 NRTI</td>
<td>PI+2NRTI</td>
</tr>
<tr>
<td>2013</td>
<td>&lt;3 years</td>
<td>Any</td>
<td>PI+2 NRTI</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td>≥3 years</td>
<td>Any</td>
<td>NNRTI+ 2 NRTI</td>
<td>PI+ 2NRTI</td>
</tr>
</tbody>
</table>
HIV drug resistance
Study flow

50 children started second-line treatment

14 children switched from first- to second-line treatment

64 children on second-line treatment were included

- missing VL during follow-up: 4
- virological suppression at last visit: 48
- treatment failure: 12

- death: 2
- 2 consecutive VL > 1000 cps/ml: 5
- last VL > 1000 cps/ml: 5
Number of children receiving ART and percentage of all children living with HIV receiving ART in low- and middle-income countries overall and by WHO region, 2013

TOTAL: 740,000
23% [21–25%]

Country income classification by the World Bank at the time of the 2011 Political Declaration on HIV and AIDS.

Fig. 2.17 Percentages of people living with HIV who were receiving ART in the WHO African region in 2005, 2010 and 2014

ART coverage (%)
- 0-9
- 10-19
- 20-39
- 40-59
- ≥60
- Data not available
- Not applicable

Sources: Global AIDS Response Progress Reporting (UNAIDS/UNICEF/WHO) and UNAIDS/WHO estimates.
Main findings

- 18.8% treatment failure after 24 months
- No PI resistance in children with treatment failure
- Treatment failure associated with underweight and poor adherence, but not with NRTI resistance at second-line initiation
Recommendations

- PI-based treatment
- Adherence support
- Long-term follow-up data
Second-line ART in children

• Limited data available

• Treatment failure in children on second-line ART:
  • 15-50% failure after 12-50 months

• Definitions of virological failure and duration of follow-up vary widely

Conclusions

- Treatment outcomes on second-line relatively good:
  - Adults:
    - 23.1% failure (meta-analysis)
    - 85% suppression (PASER cohort)
  - No PI resistance after 24 months, but:
    - Might develop in the long term
    - Adherence

Ajose et al. AIDS 2012; 26 (8)
Boender et al. Conference on Retroviruses and Opportunistic Infections (CROI) 2016. Abs #498