NDOH PAEDIATRIC 3rd LINE ART PROGRAM

Dr Mo Archary
King Edward VIII Hospital/UKZN
Paediatric Infectious Diseases unit
What’s in the Bucket?
Difference bet. the Paeds and Adult

Twenty Two year old
Failing a PI Based regimen
Difference between the Paeds and Adult

Two year old Failing a PI Based regimen

Daurinavir – only >3yrs

Dolutegravir – FDA approval >12 yrs (6-12 yrs pending)

Both are not on licensed in SA

RALTEGRAVIR

ATALANAVIR
Formulation Matters

4 yr old with:

Optimal regimen Darunavir/r + Raltegravir + AZT/3tc (+/- Etravirine)
How to give this to a child who can’t swallow tablets!!!
Clinical Case – 19 yr old

• Started D4t/3TC/EFV - ? 7yrs of age
• Changed to AZT/3TC/LPV/rtv – 13 yrs of age
• Changed to LPV/rtv + Ral – 17 yrs

• Current bloods at 19yrs:
  • CD4 count: 1 cells/ul
  • VL: 136 366 copies/ml
  • Resistance test: Extensive resistance to NRTI/NNRTI/Pis and ?Integrase inhibitors
Review of NDOH 3rd Line Applications
Total Number of Applications
2013 - 2016

- Total: 192
- 2013: 24
- 2014: 81
- 2015: 77
- 2016: 10

Total No.
Applications per Province

Total Nos.

- Eastern Cape
- Free State
- Gauteng
- KZN
- LP
- MP
- NC
- NW
- WC
• Age:
  – Ave: 8.5 yrs
  – Min: 1 yr – Max: 17 yrs

Duration on Treatment:
  Ave: 75.7 months
  Min: 1.7 months – Max: 210 months

• Weight:
  – Ave: 23 kg
  – Min: 7.8 kg – Max: 55 kg

Sex:
  Females: 36%
  Males: 61%
Western Cape DOH Experience

• In October 2014 – Management of applications for genotyping and 3rd line ART in the Western Cape was dissolved to the Provincial DOH
Applications for Genotyping to Western Cape DOH (Oct 2014 – Oct 2015)

<table>
<thead>
<tr>
<th>Paediatric</th>
<th>36 / 92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applications Approved</td>
<td>22</td>
</tr>
<tr>
<td>Genotype Provided</td>
<td>14</td>
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Compiled by Jackqueline Voget and James Nuttal
## Third line ART

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
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<tbody>
<tr>
<td>Paediatric</td>
<td>36</td>
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<tr>
<td>ART Approved</td>
<td>18</td>
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<tr>
<td>- Holding regimens</td>
<td>6</td>
</tr>
<tr>
<td>- Definitive regimen</td>
<td>12</td>
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<tr>
<td>Deceased</td>
<td>1</td>
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<tr>
<td>Sequencing incomplete</td>
<td>1</td>
</tr>
<tr>
<td>Genotype Not done yet</td>
<td>3</td>
</tr>
<tr>
<td>ART not approved (no PI mutations)</td>
<td>13</td>
</tr>
</tbody>
</table>

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3rd line Review Protocol
Indications for genotyping

- Any newly diagnosed child <2 years of age whose mother was receiving PI-based cART during pregnancy and/or during breastfeeding

- Patients on a PI regimen with virological non-suppression defined as at least 3 viral load measurements of \( \geq 30,000 \) copies/ml (\( \geq \log 4.5 \)) at least 8-12 weeks apart:
  - Children (<15 years of age): receiving PI regimen for at least 1 year
  - Adults & adolescents \( \geq 15 \) years of age: receiving PI regimen for at least 2 years
Eligibility criteria for 3rd line cART

- Accessing cART through public sector
- Lopinavir (LPV) or atazanavir (ATV) mutation score ≥15 (Stanford)
Holding Regimen

• **Is the child eligible for a holding regimen?**
  - CD4 count $\geq 350$ (\(\geq 5\) years age) / $\geq 25\%$ (\(< 5\) years of age)
  - In the interests of the child to delay switch to 3\(^{rd}\) line cART due to serious adherence issues or poor drug tolerance

• **If yes, consider using**
  - Lamivudine (3TC) monotherapy (once daily) if AZT OR ABC OR TDF mutation score is $<30$
  - AZT + 3TC + ABC if AZT AND ABC AND TDF mutation scores are all $\geq 30$

• **Monitoring while on holding regimen**
  - CD4 count & percentage: 3 monthly
  - WHO clinical stage: 3 monthly
  - VL monitoring not required

• **When to consider starting 3\(^{rd}\) line cART**
  - CD4 count drops to $<350$ / $<25\%$
  - WHO clinical stage deteriorates
  - 3\(^{rd}\) line cART may be started before the CD4 or clinical criteria are met provided adherence issues have been resolved as far as possible

• **If no, start 3\(^{rd}\) line cART**
Children <3 years of age or <10kg (Darunavir (DRV) not approved <3 years or <10kg)

If child meets above criteria for 3rd line cART, choice of 3rd line cART should be decided by committee at time of application

Is child eligible for a holding regimen?

| CD4 count ≥25% | In the interests of the child to delay switch |

If yes, consider using

| Lamivudine (3TC) monotherapy (once daily) | Consider using AZT + 3TC + ABC |

Monitoring while on holding regimen

| CD4 count & percentage: 3 monthly | WHO clinical stage: 3 monthly | VL monitoring not required |

When to consider starting 3rd line cART

| When child reaches ≥3 years of age | CD4 count drops to <25% | WHO clinical stage deteriorates | Maybe started sooner |

If still <3yrs or < 10kg, consider off-label use of 3rd line cART
Children ≥3 years of age and ≥10kg

- All get DRV/r

- All get 3TC or Emtricitabine (FTC)

- Plus either AZT OR ABC whichever has the lowest score. Consider using TDF in place of AZT OR ABC in children/adolescents weighing ≥40kg with eGFR >80

- Add Raltegravir (RAL) if
  - The AZT OR ABC OR TDF mutation score is ≥30 OR
  - The DRV mutation score is ≥15

- Add Etravirine (ETR) in addition to RAL if
  - AZT OR ABC OR TDF mutation score is ≥30 AND
  - DRV mutation score is ≥15 AND
  - ETR score is <30
Eligible for third line ART?
LPV or ATV score ≥15

DRV/r + 3TC or FTC + AZT or ABC (lowest score)

Consider using TDF in place of AZT or ABC in children/adolescents weighing ≥40kg with eGFR >80

AZT/ABC/TDF score > 30
OR
DRV ≥15

Add RAL

AZT/ABC/TDF score ≥30 + DRV ≥15 + ETR <30

Add ETR

Stanford mutation scores:
15–<30: low level resistance
30–<60: intermediate level resistance
≥60: high level resistance
Summary:

• 3rd Line committee should NOT be seen as a dictatorship
  – Queries regarding the regimen (with a rationale) / management or relevant clinical information always welcome.
  – Increasing use of standardized algorithms – improves transparency

• Willingness to devolve the responsibility to Provincial structures – provided available resources