Acquired HIV Drug Resistance in children in Asia

Jintanat Ananworanich, MD, PhD
Pediatrician/Immunologist
Deputy Director in Scientific Affairs, HIV-NAT
Chief, SEARCH
The Thai Red Cross AIDS Research Centre
Lecturer, Chulalongkorn University

Jintanat.a@hivnat.org; Jintanat.a@SearchThailand.org
Outline

- Overview pediatric HIV situation in Asia
- Prevalence of pediatric first-line failure in Asia and patterns of resistance
- Second-line treatment response and failure
- Third-line treatment
- Future needs
3.8 billion people in Asia
4.8 million living with HIV
Almost half are women
Adult prevalence 0.3%
Asian HIV Epidemic (2009)

Compared to 2005

- Children < 15 years living with HIV: 160,000
- Newly infected children: 22,000
- AIDS-related death in children: 15,000
- ART coverage: < 50%
- PMTCT coverage: < 50%

www.unaids.org
Common First-line and Second-line Regimens in the Pediatric Treat Asia cohort

April 2009 data collection
16 hospitals in 7 countries
Cambodia, China, India, Malaysia, Vietnam, Indonesia, Thailand

<table>
<thead>
<tr>
<th></th>
<th>First-line</th>
<th>Second-line</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>608</td>
<td>69</td>
</tr>
<tr>
<td>Median age</td>
<td>7 years</td>
<td>10 years</td>
</tr>
<tr>
<td>Common regimens</td>
<td>AZT/3TC/NVP - 46%</td>
<td>AZT/3TC/LPV/r - 23%</td>
</tr>
<tr>
<td></td>
<td>AZT/3TC/EFV - 26%</td>
<td>AZT/ddI/LPV/r - 21%</td>
</tr>
<tr>
<td></td>
<td>d4T/3TC/NVP - 16%</td>
<td>ddI/3TC/LPV/r - 11%</td>
</tr>
</tbody>
</table>

TREAT Asia and IeDEA Southern Africa, JIAS 2011
### Efficacy of First-line Therapy

<table>
<thead>
<tr>
<th></th>
<th>TApHOD¹</th>
<th>Cambodia²</th>
<th>China³</th>
<th>India⁴</th>
<th>Thailand⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. on ART</td>
<td>1655</td>
<td>670</td>
<td>51</td>
<td>67</td>
<td>3409</td>
</tr>
<tr>
<td>Median age at ART initiation (yr)</td>
<td>7 (4-10)</td>
<td>6 (4-8)</td>
<td>10 (7-13)</td>
<td>6 (2-10)</td>
<td>7 (5-9)</td>
</tr>
<tr>
<td>Median CD4 cells at ART initiation</td>
<td>100</td>
<td>190 (&gt;5 yo)</td>
<td>117 cells</td>
<td>225</td>
<td>104</td>
</tr>
<tr>
<td>Median CD4% at ART initiation</td>
<td>8 %</td>
<td>11 % (&lt;5yo)</td>
<td>n/a</td>
<td>12%</td>
<td>5%</td>
</tr>
<tr>
<td>Median time on ART (mo)</td>
<td>35 (18-55)</td>
<td>24 (12-34)</td>
<td>12 (18-23)</td>
<td>35 (18-23)</td>
<td>20 (12-30)</td>
</tr>
<tr>
<td>VL suppression</td>
<td>81%</td>
<td>86%</td>
<td>55%</td>
<td>n/a</td>
<td>6.6% immune failure</td>
</tr>
</tbody>
</table>

Prevalence of mutations/resistance at first and last GT

Median (IQR) duration from first to last 49 (43-120) weeks

N=303, Thai, on first line NNRTI
71 (23%) had VL > 1000

Puthanakit T, Ananworanich J. CROI 2011 [Poster 720]
# Outcome of Lopinavir/r-based Regimen for PI-naïve, NRTI/NNRTI Failure

<table>
<thead>
<tr>
<th>Location (Author, Year)</th>
<th>N</th>
<th>Baseline</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CD4</td>
<td>Viral Load</td>
</tr>
<tr>
<td><strong>Thailand</strong> (Puthanakit T, HIV Medicine 2009)</td>
<td>24</td>
<td>17%</td>
<td>4.6 log</td>
</tr>
<tr>
<td><strong>Thailand</strong> (Puthanakit T, CROI 2009)</td>
<td>241</td>
<td>10%</td>
<td>4.8 log</td>
</tr>
<tr>
<td><strong>Thailand</strong> (Bunupuradah T, Antivir Ther 2009)</td>
<td>50</td>
<td>7%</td>
<td>4.8 log</td>
</tr>
</tbody>
</table>
Third Line Therapy

- 1910 children are on ART at 8 sites in Thailand in HIV-NAT 113 study
  - 492 (26%) are on LPV/r-based second-line therapy
  - 30 (1.5%) are on/waiting for third-line

- In the Thai National Program
  - 2000-2005: 3409 treated, 4% on PI
  - 2010: 8217 treated, 1662 (20%) on second-line (most on LPV-based therapy)
    - Estimate that ≥100 children will be needing third line in the next few years

Access to ART for Treatment Failure in Asian Children

<table>
<thead>
<tr>
<th>ART</th>
<th>% Cannot access</th>
</tr>
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<tbody>
<tr>
<td>Tenofovir</td>
<td>13%</td>
</tr>
<tr>
<td>Abacavir</td>
<td>38%</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>63%</td>
</tr>
<tr>
<td>Lopinavir pediatric tablet</td>
<td>31%</td>
</tr>
<tr>
<td>Ritonavir (any formulation)</td>
<td>50%</td>
</tr>
</tbody>
</table>

No access to third-line therapy except for
- Participation in clinical trials
- Compassionate use program
  (darunavir and etravirine from Tibotec)

Limited access to viral load monitoring and genotyping

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TASER P

- Multicenter, observational cohort study to monitor virologic failure and resistance in children on second-line ART

- 300 children, 8 sites, 4 countries

- Supported by ViiV Healthcare through TREAT Asia
What do we need?

- First-line therapy

- Better options that are highly effective and easy to take
  - Fixed dose combinations, scored tablets for all drugs being manufactured
  - Once daily regimens (one pill/day for adolescents)
  - Appropriate for infants and young children

- Better access for monitoring to detect early failure and choose the best subsequent regimens (HIV RNA and genotyping)
What do we need?

- **Second-line therapy**
  - Fixed dose combinations
  - For all commonly used boosted PI (with ritonavir or GS9350)
  - Ability to monitor HIV RNA soon after switching (6 months)

- **Third-line therapy**
  - Procurement plans by national programs for new drugs (new NNRTI, PI, new classes)
  - Parallel development of pediatric formulation for all HIV drugs by pharmaceutical companies
  - More PK studies in children of different ethnicities/regions
Acknowledgement

- Dr. Sorokin Bhakeecheep (National Health Security Office, Thailand)
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- Drs. Thanyawee Puthanakit, W. Prasitsuebsai, Stephen Kerr (HIV-NAT, Bangkok)
- Treat Asia Network investigators
- PREDICT and HIV-NAT 113 Study Teams
  - Thailand: HIV-NAT/Chulalongkorn Hospital, Siriraj Hospital, Bamrasnaradura Infectious Diseases Institute, Chiang Rai Regional Hospital, Khon Kaen University, Nakornping Hospital, Prapokklao, Surin Hospital, Queen Savang Vadhana Memorial Hospital
  - Cambodia: National Pediatric Hospital, Social Health Clinic