Outcomes of children, stratified by immune status, receiving anti-retroviral therapy in Médecins Sans Frontières supported projects in resource-limited settings.

Dr Daniel O’Brien for the MSF HIV/AIDS working group
Background: paediatric HIV treatment

- 2005: 2.3 million children living with HIV, and 300,000 needing ART.
- Few children in RLS currently on ART
  - Limited experience
  - Lack of affordable simple diagnostic testing
  - Lack of affordable, adapted paediatric ARV formulations
  - Lack of paediatric FDC
  - Lack of standard paediatric dosing regimens
Background: MSF programs

- HIV/AIDS programs: 65
- Countries: 32
- Patients on ART (March 2006): 57,344
- Children < 15 years on ART: 4096 (7%)
- Collaboration with public health services
- Urban, semi-urban and rural settings
Objectives

- To assess treatment outcomes in children given ART under routine MSF program conditions according to baseline immunological status.
Definitions

- Profound immunosuppression
  \( \Rightarrow \) CD4 <5%

- Severe immunosuppression
  \( \Rightarrow \) CD4 ≥5% + <15%

- Mild-moderate immunosuppression
  \( \Rightarrow \) CD4 ≥15%
Methods

- Multi-centric analysis of data collected using a standardized data collection software (FUCHIA)
- Study period: Dec 2001 - March 2006
- Eligibility criteria
  - Project ≥30 children
  - Age 18-59 months
  - ART and available baseline CD4 data
Study cohort

- Children in MSF cohort: 16,077
- Children started on ART: 4654 (29%)
- Study population
  - Age 18-59 months on ART: 1458
  - Exclusion:
    - Project <30 children: 121
    - No CD4% at baseline: 581
  - Total included in the analysis: 756

- 23 projects in 12 countries: 8 in Africa, 2 in Asia, and 2 in Central America
## Baseline characteristics by CD4% group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline CD4%</th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5%</td>
<td>≥5%-%&lt;15%</td>
<td>≥15%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=101</td>
<td>N= 468</td>
<td>N= 187</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>37 (37%)</td>
<td>215 (46%)</td>
<td>92 (49%)</td>
<td></td>
</tr>
<tr>
<td>Median age yrs</td>
<td>3.6</td>
<td>3.1</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>{IQR}</td>
<td>{2.9-4.3}</td>
<td>{2.3-4.1}</td>
<td>{2.3-4.1}</td>
<td></td>
</tr>
<tr>
<td>Median weight kg</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>{IQR}</td>
<td>{9.5-13.1}</td>
<td>{9.8-13}</td>
<td>{9.5-14}</td>
<td></td>
</tr>
<tr>
<td>CDC stage B</td>
<td>36 (36%)</td>
<td>142 (30%)</td>
<td>73 (42%)</td>
<td></td>
</tr>
<tr>
<td>CDC stage C</td>
<td>42 (42%)</td>
<td>178 (38%)</td>
<td>65 (37%)</td>
<td></td>
</tr>
<tr>
<td>ARV naive</td>
<td>100 (99%)</td>
<td>461 (99%)</td>
<td>176 (94%)</td>
<td></td>
</tr>
</tbody>
</table>
## Duration of follow-up on ART by CD4% group

<table>
<thead>
<tr>
<th>CD4% Group</th>
<th>Median (IQR) months</th>
<th>≥12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4% &lt;5% N=101</td>
<td>13.3 (4.9-19.3)</td>
<td>54 (53%)</td>
</tr>
<tr>
<td>CD4% ≥5% - &lt;15% N=468</td>
<td>10.3 (4.0-17.9)</td>
<td>207 (44%)</td>
</tr>
<tr>
<td>≥15% N=187</td>
<td>8.4 (3.1-18.4)</td>
<td>78 (42%)</td>
</tr>
</tbody>
</table>
## Outcomes by CD4% group

<table>
<thead>
<tr>
<th></th>
<th>&lt;5% N=101</th>
<th>CD4% ≥5%-%&lt;15% N=468</th>
<th>≥15% N=187</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive on ART</td>
<td>81 (80%)</td>
<td>392 (84%)</td>
<td>157 (84%)</td>
</tr>
<tr>
<td>Dead</td>
<td>12 (12%)</td>
<td>18 (4%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2 (2%)</td>
<td>35 (8%)</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>ART stopped</td>
<td>3 (3%)</td>
<td>7 (2%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Transferred out</td>
<td>3 (3%)</td>
<td>12 (3%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0%)</td>
<td>4 (1%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>
Deaths by time on ART (n=36)

- < 6 months: 78%
- 6-12 months: 11%
- 12-24 months: 6%
- 24-36 months: 6%

Median time on ART at death: 1.5 months (IQR 0.6 – 5.3)
## Survival by baseline CD4% group (end point: deaths + LFU)

<table>
<thead>
<tr>
<th>Time</th>
<th>&lt;5%</th>
<th>CD4% ≥5%–&lt;15%</th>
<th>≥15%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=101</td>
<td>n=468</td>
<td>n=187</td>
</tr>
<tr>
<td>6 months</td>
<td><strong>0.89 (0.89-0.94)</strong></td>
<td><strong>0.94 (0.92-0.96)</strong></td>
<td><strong>0.93 (0.88-0.96)</strong></td>
</tr>
<tr>
<td>(95% CI)</td>
<td>n=70</td>
<td>n=315</td>
<td>n=110</td>
</tr>
<tr>
<td>12 months</td>
<td><strong>0.88 (0.79-0.93)</strong></td>
<td><strong>0.91 (0.88-0.94)</strong></td>
<td><strong>0.91 (0.85-0.95)</strong></td>
</tr>
<tr>
<td>(95% CI)</td>
<td>n=54</td>
<td>n=207</td>
<td>n=78</td>
</tr>
<tr>
<td>24 months</td>
<td><strong>0.84 (0.73-0.91)</strong></td>
<td><strong>0.82 (0.75-0.87)</strong></td>
<td><strong>0.86 (0.77-0.92)</strong></td>
</tr>
<tr>
<td>(95% CI)</td>
<td>n=12</td>
<td>n=54</td>
<td>n=15</td>
</tr>
</tbody>
</table>
Probability of survival
(end point: death + LFU) by baseline CD4% group at ART initiation

Log rank test $p=0.6$
Median CD4% gain after ART initiation by study group

- Median Gain CD4% 6 months: (n=177, 36%)
- Median Gain CD4% 12 months: (n=174, 52%)
- Median Gain CD4% 18 months: (n=73, 38%)

- CD4<5%
- CD4>5&<15
- CD4>15%
Proportion CD4% <15 after ART by study group

- **Baseline** (n=569): 100%
- **6 months** (n=138, 36%): 57%
- **12 months** (n=134, 51%): 24%

% with CD4% <15

- **CD4%<5**
- **CD4%>5&<15**
Proportion CD4% >25 after ART by study group

% with CD4% >25

Baseline (n=756) 6 months (n=177, 36%) 12 months (n=174, 52%)

CD4%<5 32 28
CD4%>5&<15 42 62
CD4%>15 74 83
Limitations

- Surveillance multicentric data
- Relatively short follow-up
- Limited information on immunological outcomes
- No virological outcomes
Conclusions

- Very satisfactory treatment outcomes for children with profound and severe immunosuppression in resource limited settings
- Extent immunosuppression at baseline for ART does not appear to impact on short-term treatment outcomes
Acknowledgments

- Ministries of Health
- MSF program staff
- Epicentre, Paris
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