Introduction of ART in a community based cohort in Uganda and its impact on HIV related mortality

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Introduction

• There are encouraging global efforts to scale up availability of ART in developing countries with high HIV burden

• There is uncertainty about the feasibility of ART in developing country settings

• The benefits of ART in developing country settings have not been widely documented

• We present a historical comparison of HIV related mortality rates before and after introduction of ART in a Ugandan cohort
Background: the Entebbe cohort

- Set up in 1995, initially to evaluate a pneumococcal vaccine in HIV-1 infected adults
- Enrolls adults with HIV infection, age 15 – 59 residing in and around Entebbe who consent to participate. WHO stage IV excluded.
- Aims to evaluate interventions that reduce progression to AIDS or death
- The cohort has so far enrolled 2766 participants with 5942.7 person years of observation
CD4 at enrolment into the Entebbe Cohort

Number enrolled

Year of enrolment into Entebbe Cohort

- <200
- 200-500
- >500

XV World AIDS, 2004
Background: the DART trial

- A randomised trial of monitoring practice and structured treatment interruptions
- Started in February 2003
- Enrolls symptomatic ARV naïve adults with CD4<200 cells/mm³, aged 18 years or more, residing in and around Entebbe, who fulfill clinical criteria for ART and consent to participate
- All members of Entebbe cohort eligible for ART were put onto DART
CD4 at enrolment into the DART Trial

<table>
<thead>
<tr>
<th>Years</th>
<th>Number enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>100 - 199</td>
</tr>
<tr>
<td>2004</td>
<td>0 - 49</td>
</tr>
</tbody>
</table>

Legend:
- Red: 0 - 49
- Orange: 50 - 99
- Green: 100 - 199
Methods: Enrolment procedures

**Entebbe Cohort**
- Contact information
- Confirmatory HIV test
- WHO clinical staging
- Appropriate management of current illness
- FBC, CD4/CD8

**DART Trial**
- Contact information
- Confirmatory HIV test
- WHO clinical staging
- Appropriate management of current illness
- FBC, Biochemistry, CD4/CD8
- **Triple Therapy ART**
Methods:
Follow up procedures

Entebbe Cohort
- Follow up every 6 mnths
- Document clinical events
- WHO clinical staging
- FBC, CD4/CD8
- Plasma and serum storage
- Extra visits for acute clinical events
- Deaths recorded

DART Trial
- Follow up every 4 wks
- Document clinical events
- FBC, biochemistry
- CD4/CD8 12 wkly
- Check adherence to ART
- Plasma storage 12 wkly
- Extra visits for acute clinical events
- Deaths recorded
Methods: Analysis

Entebbe Cohort

- observation period
  May 1995 to Jan 98

to match DART population data
restricted to
- CD4 < 200 at enrolment
- Hb >8mg/dl
- neutrophils >0.5x10^9/l

DART Trial

- observation period
  Feb 2003 to May 2004

3 patients contribute time at risk in both Entebbe Cohort and the DART Trial
Results I

- Compare the death rate during the first 27 months of follow up in the Entebbe Cohort to that during the first 15 months of the DART trial

<table>
<thead>
<tr>
<th></th>
<th>Entebbe Cohort</th>
<th>DART Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of observation</td>
<td>May 95 - Jan 98</td>
<td>Feb 03 - May 04</td>
</tr>
<tr>
<td>Total number of subjects</td>
<td>456</td>
<td>745</td>
</tr>
<tr>
<td>Total person years of follow up</td>
<td>347</td>
<td>358</td>
</tr>
<tr>
<td>Total number of deaths</td>
<td>211</td>
<td>20</td>
</tr>
</tbody>
</table>
## Results II

<table>
<thead>
<tr>
<th>Baseline CD4 count</th>
<th>Entebbe Cohort</th>
<th>DART Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of subjects</td>
<td>Person years of f/u</td>
</tr>
<tr>
<td>0-49</td>
<td>171</td>
<td>96</td>
</tr>
<tr>
<td>50-99</td>
<td>109</td>
<td>85</td>
</tr>
<tr>
<td>100-199</td>
<td>176</td>
<td>166</td>
</tr>
<tr>
<td>Total</td>
<td>456</td>
<td>347</td>
</tr>
</tbody>
</table>
## Results III

<table>
<thead>
<tr>
<th>Entebbe Cohort</th>
<th>DART Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline CD4 count</td>
<td>Death rate per 1000 py</td>
</tr>
<tr>
<td>0-49</td>
<td>975.3</td>
</tr>
<tr>
<td>50-99</td>
<td>662.5</td>
</tr>
<tr>
<td>100-199</td>
<td>367.7</td>
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<tr>
<td>Total</td>
<td>608.4</td>
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Discussion

• Previous study interventions within the Entebbe cohort may have contributed to the observed reduction in mortality
  – Cotrimoxazole prophylaxis study
    Aug 2000 to Feb 2002 and continued
  – INH prophylaxis study Nov 1998 to Oct 1999

• Adherence to therapy reinforced in a clinical research setting
Conclusion

- The introduction of ART in this Ugandan cohort is associated with a significant reduction in HIV related mortality.

- Initiation of ART even in those most severely immunosuppressed (CD4 <50 cells/mm³) is still highly beneficial.
Appreciation

- Study participants
- TASO Entebbe
- Entebbe Study teams
- MRC UK; DFID
- Boehringer Ingelheim; Glaxo Smith Kline
  and Gilead