



# Survival and Causes of Death, 2 years after introduction of Antiretroviral Therapy in Africa: a historical cohort comparison in Entebbe, Uganda

Munderi P., Watera C., Nakiyingi J., Kasirye A.,  
Walker S., French N., Gilks C., Grosskurth H.

on behalf of the **DART** trial team

# Introduction

- Data on the effectiveness and impact of ART are essential for informing treatment in Africa
- There are few reports from Africa
  - Mostly observational ART cohorts / short term
- We compared 2 year survival and causes of death among patients in an ART trial, with that in a matched pre-ART historical cohort

# Cohort Procedures



## Pre-ART: Entebbe Cohort

- Established 1995
- Clinical follow up 6 monthly
- CD4 6 monthly
- Extra visits for acute clinical events
- Deaths recorded and reviewed by physician

## Post-ART: DART Trial

- Enrollment from Feb 2003
- Clinical follow up every month
- CD4 3 monthly
- Extra visits for acute clinical events
- Deaths recorded and reviewed by committee



# Observation Periods

	<b>Pre-ART: Entebbe Cohort</b>	<b>Post-ART: DART Trial</b>
Period of observation	Oct 95 - Dec 00	Feb 03 - Jan 06
Total number of subjects	<b>516</b>	<b>1015</b>
Total person years of follow-up	658	1819

# Characteristics at Enrollment



	Pre-ART Entebbe Cohort (n=516)		Post-ART DART (n=1015)	
<b>Sex</b>				
male	169	(33%)	334	(33%)
female	347	(67%)	681	(67%)
<b>Age (years)</b>				
mean (SD)	31.5	(7.2)	37.0	(7.9)
<b>CD4 (cells/mm<sup>3</sup>)</b>				
0-49	199	(38%)	328	(32%)
50-99	122	(24%)	220	(22%)
100-149	114	(22%)	241	(24%)
150-199	81	(16%)	226	(22%)
median (IQR)	75	(23-130)	93	(31-145)

# Number of Deaths



62 deaths occurred in DART

380 deaths occurred in the pre-ART cohort

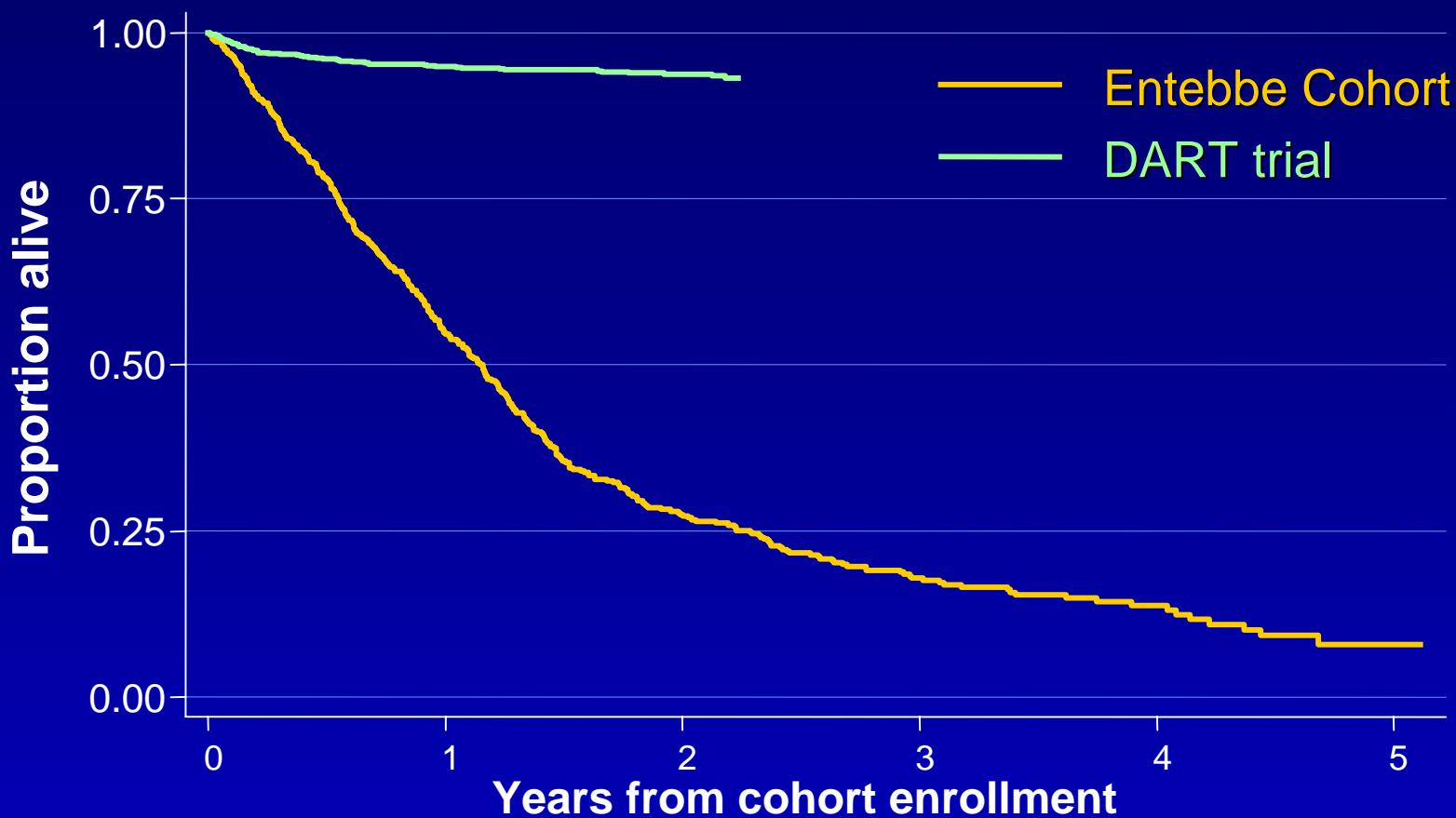
Aprox. half the deaths in CD4 < 50 category

# Death Rates by CD4 at Enrollment



Baseline CD4 count	Pre-ART: rate/1000 PY	Post-ART: rate/1000PY	RR	p
0-49	953	60	15.8	<0.001
50-99	626	25	25.3	<0.001
100-149	447	18	24.9	<0.001
150-199	278	25	11.3	<0.001
Overall	577	34	16.9	<0.001

# Survival



Proportion alive (by cohort and CD4 at enrollment)

EC, <50	1.00	0.38	0.12
EC, >50	1.00	0.65	0.36
DART, <50	1.00	0.91	0.89
DART, >50	1.00	0.97	0.96

# Causes of Death



	Pre-ART: EC		Post-ART: DART	
	Deaths (rate/100PY)		Deaths (rate/100PY)	
<b>Specific HIV-related causes</b>	<b>118</b>	<b>(17.9)</b>	<b>27</b>	<b>(1.5)</b>
<b>Cryptococcus</b>	<b>64</b>	<b>(9.7)</b>	<b>4</b>	<b>(0.2)</b>
Cryptosporidium	18	(2.7)	2	(0.1)
<b>Tuberculosis</b>	<b>16</b>	<b>(2.4)</b>	<b>10</b>	<b>(0.5)</b>
HIV-related malignancy	11	(1.7)	6	(0.3)
Bacteraemia	3	(0.5)	5	(0.3)
CMV	4	(0.6)	0	(0)
Severe anaemia	2	(0.3)	0	(0)
<b>Syndrome likely HIV related</b>	<b>176</b>	<b>(26.7)</b>	<b>18</b>	<b>(1.0)</b>
<b>Wasting (+/- diarrhoea)</b>	<b>111</b>	<b>(16.9)</b>	<b>1</b>	<b>(0.1)</b>
Febrile event	48	(7.3)	12	(0.7)
Neurological event	17	(2.6)	5	(0.3)
<b>Cause not HIV-related</b>	<b>4</b>	<b>(0.6)</b>	<b>6</b>	<b>(0.3)</b>
<b>Unknown cause</b>	<b>82</b>	<b>(12.6)</b>	<b>11</b>	<b>(0.6)</b>
<b>Total deaths</b>	<b>380</b>	<b>(57.7)</b>	<b>62</b>	<b>(0.3)</b>

# Discussion



- Historical comparison - need to be cautious in interpretation
- Differences in follow up between the 2 cohorts
- Up to 22% 'unknown' cause of death
- Some effect may be due to other improvements in health care over time - e.g. cotrimoxazole
- Observed impact is in a clinical research setting with excellent follow up and adherence

# Conclusion

- First-line ART is highly effective
  - 2 year survival on ART is **94%**
  - Overall mortality reduced **17-fold** compared to a matched pre-ART cohort
  - Significant survival benefit even when treatment initiated at very low CD4 counts
- Substantial reductions in deaths associated with common opportunistic pathogens
- Disappearance of HIV wasting as a syndrome around death
- TB, HIV related malignancy and Bacteraemia remain important causes of mortality in the ART era

# Appreciation



- Study participants
- TASO Entebbe
- DART Study teams
  
- MRC UK ; DFID ; Rockefeller Foundation
  
- Donation of study drugs from
  - Boehringer Ingelheim
  - GlaxoSmithKline
  - Gilead Sciences



# Thank You