



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

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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

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

Characteristics at Enrollment



	Pre-ART Entebbe Cohort (n=516)		Post-ART DART (n=1015)	
Sex				
male	169	(33%)	334	(33%)
female	347	(67%)	681	(67%)
Age (years)				
mean (SD)	31.5	(7.2)	37.0	(7.9)
CD4 (cells/mm³)				
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

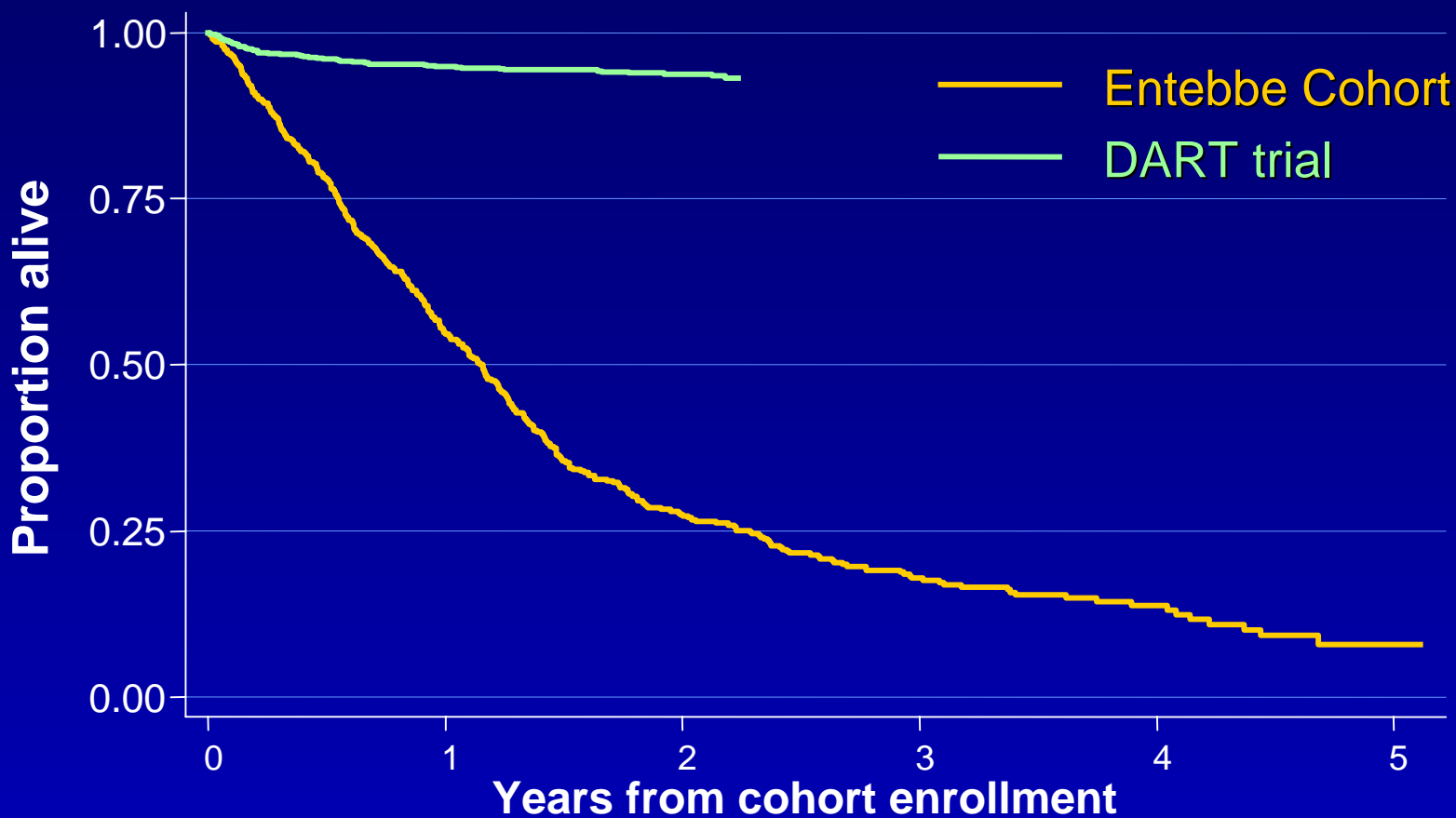
Aprox. half the deaths in CD4 < 50 category

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)	
Specific HIV-related causes	118	(17.9)	27	(1.5)
Cryptococcus	64	(9.7)	4	(0.2)
Cryptosporidium	18	(2.7)	2	(0.1)
Tuberculosis	16	(2.4)	10	(0.5)
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)
Syndrome likely HIV related	176	(26.7)	18	(1.0)
Wasting (+/- diarrhoea)	111	(16.9)	1	(0.1)
Febrile event	48	(7.3)	12	(0.7)
Neurological event	17	(2.6)	5	(0.3)
Cause not HIV-related	4	(0.6)	6	(0.3)
Unknown cause	82	(12.6)	11	(0.6)
Total deaths	380	(57.7)	62	(0.3)

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