Pregnancy rates & Outcomes among women on triple-drug antiretroviral therapy in the DART trial

Paula Munderi[1]; Helen Wilkes[2]; Dinah Tumukunde[3]; Ennie Chidziva[4]; Ruth Nalumenya[5]; Charles Gilks[6]; Eva Zalwango[1]; Moira Spyer[2]; Harriet Kyomugisha[3]; Fred Lutwama[5]; Ben Kikaire[1]; Cissy Kityo[3]; Andrew Reid[4]; Diana Gibb[2] and the DART Trial Team

[1]MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda; [2] MRC Clinical Trials Unit, London, UK; [3] Joint Clinical Research Centre, Kampala, Uganda; [4] University of Zimbabwe Clinical Research Centre, Harare, Zimbabwe; [5] Infectious Diseases Institute, Kampala, Uganda; [6] Imperial College London, UK

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BACKGROUND

Systematic data on the occurrence of pregnancy and outcomes of pregnancy among African women on combination antiretroviral therapy (ART) are scarce

2156 of women were enrolled in the Ugandan / Zimbabwean DART trial of whom 1867 (87%) were of child-bearing age

- <45 years at enrolment; median age 35 years

No women were pregnant at enrolment into the trial

Women in DART were:

- encouraged to avoid unwanted pregnancy
- given contraceptive advice (including free condoms)
- encouraged to seek counselling if wishing to conceive
- encouraged to disclose any pregnancy

Women who became pregnant during the DART trial:

- continued ART (regimens modified if indicated)
- continued in study randomised allocation
- had extra visits to study clinics as needed and extra diagnostic tests as required for pregnancy care
- were referred for antenatal, birth & postnatal care

METHODS

Pregnancy tests were routinely performed every 6 months

Systematic recording of :

- Incident pregnancies and pregnancy outcomes
- Infant outcomes at birth
- Infant feeding choice
- Infant infection status if tested

Data on follow up of mothers from Jan 2003 to June 2009 analysed for:

- Pregnancy incidence over time on ART
- Pregnancy incidence by maternal age
- Effect of baseline CD4 count & WHO stage on pregnancy rates

Data on infant follow up to from 2 weeks of age are analysed for:

- Congenital abnormalities
- Early infant survival
- HIV infection status if teted

Longer term infant follow up & documentation of infant outcomes are ongoing under separate sub-study

RESULTS

Median follow-up 4.6 years

378 pregnancies in 299 women:

- 1 pregnancy 235
- 2 pregnancies 50
- 3 pregnancies 13
- 4 pregnancies 1

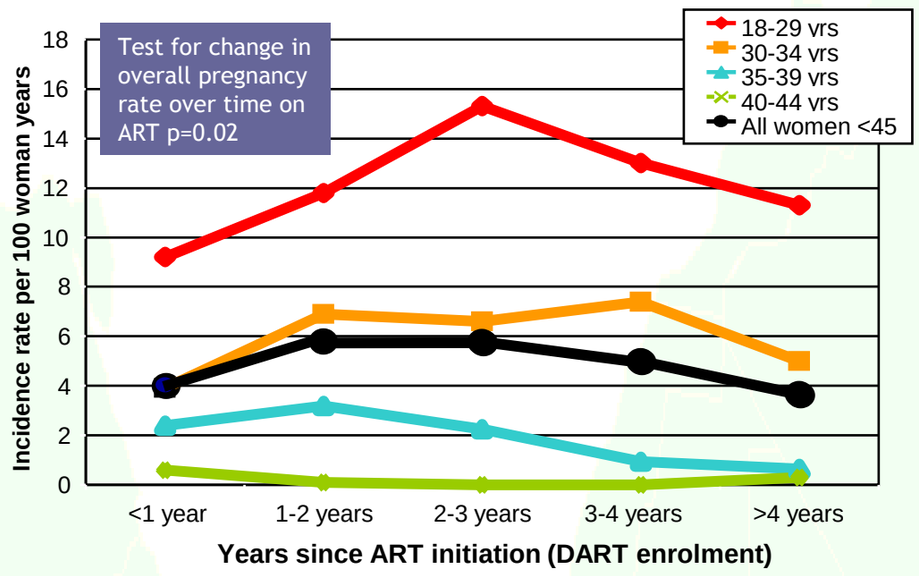
One or more pregnancies in:

- 16% women aged <45 years
- 33% women aged <30 years
- similar across study centres

Overall pregnancy rate in women < 45 years of age:

- 4.83 /100 woman-years [95% CI 4.36-5.34]

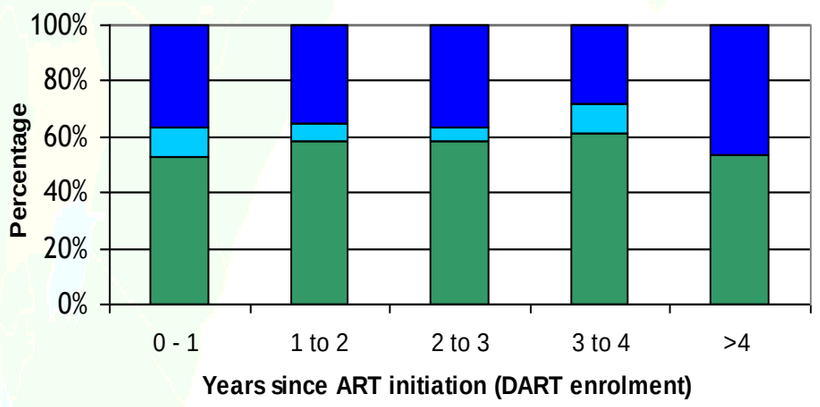
INCIDENCE OF PREGNANCY BY AGE & TIME SINCE ENROLMENT



EFFECT OF BASELINE CD4 COUNT & WHO STAGE ON PREGNANCY RATES

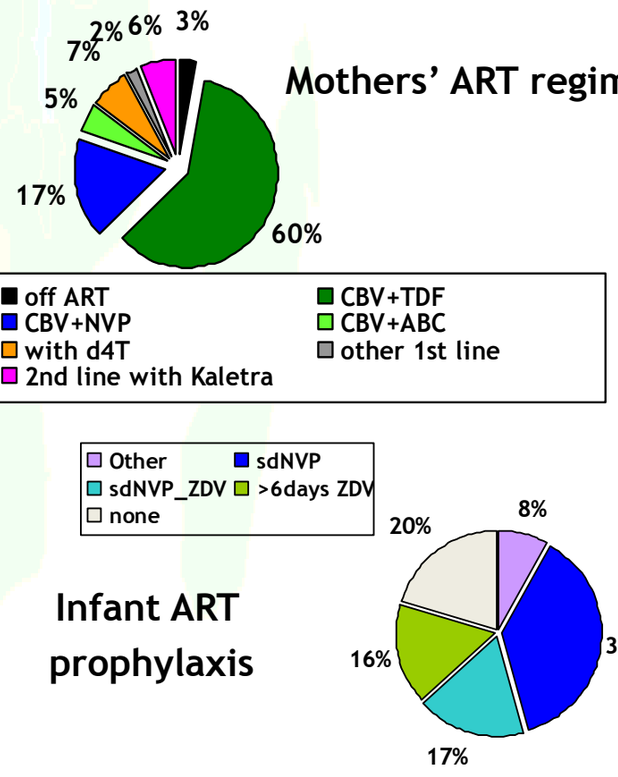
	Never pregnant N=1568	Ever pregnant N=299	All women <45 yrs N=1867	P value
Median CD4 count (median,(IQR))	87 (31-141)	106 (42-152)	90 (32-142)	0.01
WHO Stage II (n,%)	326 (21%)	68 (23%)	394 (21%)	
WHO Stage III (n, %)	830 (53%)	182 (61%)	1012 (54%)	
WHO Stage IV (n,%)	412 (26%)	49 (16%)	461 (25%)	0.001

PREGNANCY OUTCOMES OVER TIME ON ART



No significant difference in rates over time (p=0.63)

MATERNAL AND INFANT ART



ZDV - Zidovudine; CBV - Combivir; TDF - Tenofovir; ABC - Abacavir; NVP - Nevirapine; d4T - Stavudine; sdNVP - Single Dose Nevirapine

MATERNAL OUTCOMES

4 mothers died

- 2 during pregnancy: one severe malaria; one septic abortion
- 2 peripartum: one post-partum haemorrhage; one puerperal psychosis

FOETAL & INFANT OUTCOMES

206 live births and 26 stillbirths

Any congenital abnormality reported	**7 (3.0%)**
▪ Congenital talipes (club foot)	3 (2TDF, 1NVP)
▪ Congenital hydrocephalus	1 (died) (TDF)
▪ Cardiac (PDA and ASD)	1 (NVP)
▪ Undescended testes	1 (NVP)
▪ Skin tag on neck	1 (TDF)
Prematurity (gestation <37 weeks):	
▪ among live births only	9%
▪ among live and stillbirths	16%
Low birthweight (<2500 gm)	
▪ among all live births only	17%
▪ among live births ≥37 weeks	13%
▪ mean (SD) weight in babies >37 weeks = 3.0 (0.54) Kg	
9 neonatal deaths were reported by 2 weeks postpartum	
▪ foetal distress	(2)
▪ prematurity	(1)
▪ intestinal obstruction	(1)
▪ haemorrhagic disease	(1)
▪ unknown	(4)

- 6 of these neonatal deaths occurred within 24 hours of birth
- 5 were HIV-DNA PCR/antibody negative, 4 were not tested

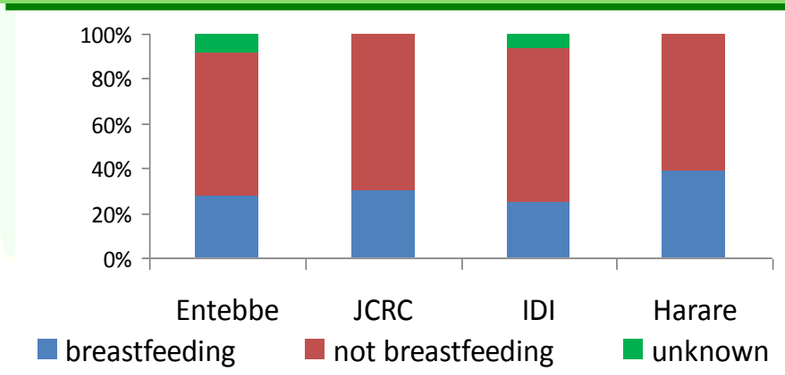
HIV infection status at two week visit

Only a small minority, 15 (7%), had been tested by the DART assessment visit at two weeks; none of these was HIV infected.

174/206 infants are enrolled into the separate infant follow up study.

152 of these are known to be still alive. Of the 137/174 (79%) for whom test results are available, none are HIV infected. The study is ongoing.

INFANT FEEDING CHOICE AT TWO WEEKS



~30% of infants breastfed at all study sites

CONCLUSIONS & RECOMMENDATIONS

- Pregnancy rates in this population of HIV-infected African women increased after the 1st year on ART and declined from the 4th year on ART
- Rates of pregnancy were higher among the younger age group and among women with less severe HIV clinical disease
- High rates of foetal loss were observed and are constant over time. This may be due to improved reporting in the clinical study setting; however, increased foetal loss in HIV-infected women has been reported in other studies
- Rates of congenital abnormalities in this study are low and similar to those previously reported
  - 3.0/100 (2.4-3.7) HIV-infected women with first trimester ART in the Antiretroviral Pregnancy Register
  - 2.7/100 live births in the CDC birth defects register
- Few women in DART chose to breastfeed
- No baby from this cohort is known to be HIV-infected
- Continued documentation and outcome event monitoring from similar treatment cohorts is necessary. This will contribute to the knowledge base on the effects of antiretroviral therapy on pregnancy, the neonatal period, early infancy & childhood.

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