

97% Progression Free Survival of HIV Positive Pregnant Women 33 Months Post Delivery - London HIV Perinatal Research Group (LHPRG)

F Martin^{1,2}, L Navaratne³, W Khan⁴, L Sarner⁵, D Mercey⁶, J Anderson², H Noble⁵, A Fakoya⁵, DA Hawkins⁴, A de Ruiter³, GP Taylor⁷

St Mary's NHS Trust¹, Homerton University NHS Trust², Guy's and St Thomas' NHS Foundation Trust³, Chelsea & Westminster Hospital⁴, Newham Healthcare NHS Trust⁵, Mortimer Market Centre University College Hospital⁶, Imperial College, London, UK

Objectives:

To document the post-partum disease-free survival of HIV positive women who took antiretroviral therapy (ART) during pregnancy.

To assess if using zidovudine monotherapy (ZDVm) during pregnancy, according to British HIV Association (BHIVA) Guidelines for the prevention of MTCT, adversely affected long-term maternal clinical outcome.

Methods:

Prospective audit of all HIV positive pregnant women who received antiretroviral therapy as part of interventions to reduce MTCT from 1998 to 2002 at six London Hospitals.

Followed-up for a minimum of 3 months.

Outcome data:
 CD4 lymphocyte count
 HIV RNA copies/ml plasma (VL)
 Need for anti-retroviral treatment
 Clinical Status

Main analysis:

HIV positive pregnant women who took either ZDVm or a combination of three or more drugs (CART) during their first completed pregnancy were analysed and compared prospectively.

Sub-analysis:

A subgroup of patients in the CART group who received short-term combination antiretroviral therapy (START) for the prevention of MTCT during pregnancy were identified and compared with mothers in the ZDVm group retrospectively.

Results: Characteristics of Cohort

311 HIV positive pregnant women were included for analysis (Graph 1):

85 women received ZDVm during pregnancy

226 women received CART during pregnancy

71/226 women received START during pregnancy

Another 49 mothers who were followed up for less than three months after delivery were excluded.

Demographics are presented in Graphs 2 and 3.

Median parity was one (1-7), median gestation at 1st antenatal clinic (ANC) attendance and delivery were

16 (3-38) and 38 (25-43) weeks.

10 patients developed pre-eclampsia (1= ZDVm and 9 = CART).

Mode of delivery: 72% Pre-labour C-section (ZDVm= 80%, CART= 70%)

16% Emergency C-section (ZDVm= 13%, CART= 16%)

11% Spontaneous vaginal delivery (ZDVm= 6.7%, CART= 13%)

1 out of 342 babies was HIV positive.

Follow up (Graph 4): mean of 33 and median of 30 months (3.1-75.5) = total of 848 person-years.

Results: ZDVm compared with CART

CD4+ lymphocyte count (Graph 5):

The CD4 count was significantly higher in patients who received received ZDVm compared to CART, both at the 1st ANC and at delivery (p < 0.001) and at last FU (p= 0.02).

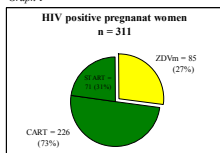
HIV RNA copies/ml plasma (Graph 6):

At 1st ANC the women offered ZDVm, because of their low VL, had a median VL ten fold less than women who received CART (p<0.001). This difference was no longer present at delivery or at last FU (p= 0.8 and p= 0.2), when the median VL in both groups was below the lower limit of detection (<1.7 log copies).

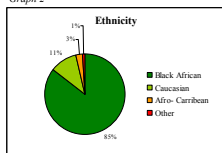
References:

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- 5 French R, Brocklehurst P. The effect of pregnancy on survival in women infected with HIV: a systematic review of literature and meta-analysis. *British Journal of Obstetrics and Gynaecology* 1998, 105: 827-835.

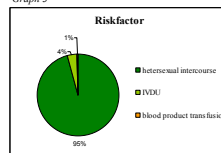
Graph 1



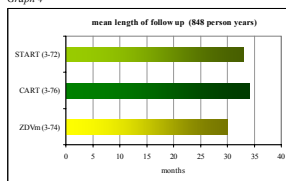
Graph 2



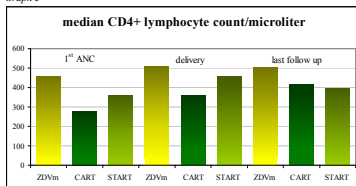
Graph 3



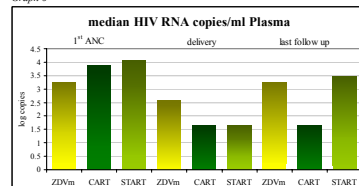
Graph 4



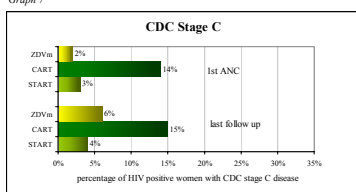
Graph 5



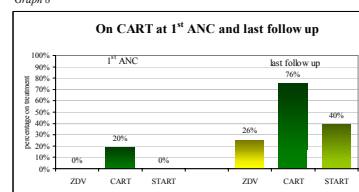
Graph 6



Graph 7



Graph 8



Clinical progression (Graph 7):

CDC Staging at 1st ANC attendance (Graph 7): CDC A = 72%, CDC B = 16%, CDC C = 11%

There was no statistical difference in the CDC progression between the treatment groups.

At last FU only eight patients had progressed clinically: Three patients group progressed to CDC stage C in the ZDVm. In the CART group two patients progressed to CDC stage B and three to CDC stage C.

AIDS defining illnesses (ADI):
 pulmonary tuberculosis (three patients)
 military tuberculosis
 pneumocystis pneumonia
 ADI unknown

One maternal death occurred due to severe lactic acidosis 14 days post delivery in the CART group.

Treatment (Graph 8):

Of all women analysed 265/311 (85%) women were treatment naive at 1st ANC. 193/311 (62%) were receiving CART at last FU. There was no significant difference in the response to treatment between ZDVm and CART group (p= 0.7).

Only a quarter of the women treated with ZDVm during pregnancy needed CART for their own health at last FU with 91% of them responding well to treatment (CD4 > 200 cells/µl and VL < 50 HIV RNA cop/ml).

Results: ZDVm compared with START

A treatment naive subgroup of CART patients was treated with ART during their pregnancies for prevention of MTCT only and stopped after delivery. We compared these patients, short-term combination antiretroviral therapy (START, n = 71), with the ZDVm group.

CD4+ lymphocyte counts (Graph 5):

The median nadir and 1st ANC CD4 counts were significantly lower in the START than the ZDVm group (p<0.001). This difference had disappeared at the time of delivery and at last FU. The median CD4+ lymphocyte count was lower in the START group compared to the ZDVm group at last FU (p= 0.02).

HIV RNA copies/ml plasma (Graph 6):

As expected the VLs were significantly different between the two groups at 1st ANC (p= 0.004). This difference had disappeared at the time of delivery and at last FU.

Clinical progression (Graph 7):

There was no significant difference in clinical progression between the two groups. One mother in the START group progressed to CDC stage C (ADI = Pulmonary TB) compared to 3 mothers in the ZDVm (p= 1).

Treatment (Graph 8):

At last FU 28 women (40%) in the START and 22 (20%) in the ZDVm groups were now taking CART (p= 0.1). There was no significant difference in their response to antiretroviral treatment (p= 0.2).

Conclusion:

In our study: 97% of all mothers had no progression of CDC stage during 848 person-years of FU.

Women who took ART during pregnancy and had continued access to CART had a favourable outcome during almost 3 years of FU.

This applied equally to mothers offered short term ZDVm or CART according to British HIV Association (1998 and 2001) guidelines.

Treatment naive mothers treated during their pregnancy with ZDVm as well as mothers treated with short term CART (START) purely to prevent MTCT were:

- no more likely to have an opportunistic infection
- no less likely to respond to subsequent antiretroviral treatment during their follow up than women who continued CART after pregnancy.

Selective use of ZDVm during pregnancy in women with good immune function and low viral load remains a valid option to prevent MTCT (in women choosing to deliver by Pre-labour C-section) for mother and baby.