Abstract:

BACKGROUND: Breastfeeding is essential for child health and development in low-resource settings but carries a significant risk of transmission of HIV-1, especially in late stages of maternal disease. We aimed to assess the efficacy and safety of triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis in pregnant women infected with HIV. METHODS: Pregnant women with WHO stage 1, 2, or 3 HIV-1 infection who had CD4 cell counts of 200-500 cells per μL were enrolled at five study sites in Burkina Faso, Kenya, and South Africa to start study treatment at 28-36 weeks' gestation. Women were randomly assigned (1:1) by a computer generated random sequence to either triple antiretroviral prophylaxis (a combination of 300 mg zidovudine, 150 mg lamivudine, and 400 mg lopinavir plus 100 mg ritonavir twice daily until cessation of breastfeeding to a maximum of 6·5 months post partum) or zidovudine and single-dose nevirapine (300 mg zidovudine twice daily until delivery and a dose of 600 mg zidovudine plus 200 mg nevirapine at the onset of labour and, after a protocol amendment in December, 2006, 1 week post-partum zidovudine 300 mg twice daily and lamivudine 150 mg twice daily). All infants received a 0·6 mL dose of nevirapine at birth and, from December, 2006, 4 mg/kg twice daily of zidovudine for 1 week after birth. Patients and investigators were not masked to treatment. The primary endpoints were HIV-free infant survival at 6 weeks and 12 months; HIV-free survival at 12 months in infants who were ever breastfed; AIDS-free survival in mothers at 18 months; and serious adverse events in mothers and babies. Analysis was by intention to treat. This trial is registered with Current Controlled Trials, ISRCTN71468401. FINDINGS: From June, 2005, to August, 2008, 882 women were enrolled, 824 of whom were randomised and gave birth to 805 singleton or first, liveborn infants. The cumulative rate of HIV transmission at 6 weeks was 3·3% (95% CI 1·9-5·6%) in the triple antiretroviral group compared with 5·0% (3·3-7·7%) in the zidovudine and single-dose nevirapine group, and at 12 months was 5·4% (3·6-8·1%) in the triple antiretroviral group compared with 9·5% (7·0-12·9%) in the zidovudine and single-dose nevirapine group (p=0·029). The cumulative rate of HIV transmission or death at 12 months was 10·2% (95% CI 7·6-13·6%) in the triple antiretroviral group compared with 16·0% (12·7-20·0%) in the zidovudine and single-dose nevirapine group (p=0·017). In infants whose mothers declared they intended to breastfeed, the cumulative rate of HIV transmission at 12 months was 5·6% (95% CI 3·4-8·9%) in the triple antiretroviral group compared with 10·7% (7·6-14·8%) in the zidovudine and single-dose nevirapine group (p=0·02). AIDS-free survival in mothers at 18 months will be reported in a different publication. The incidence of laboratory and clinical serious adverse events in both mothers and their babies was similar between groups. INTERPRETATION: Triple antiretroviral prophylaxis during pregnancy and breastfeeding is safe and reduces the risk of HIV transmission to infants. Revised WHO guidelines now recommend antiretroviral prophylaxis (either to the mother or to the baby) during breastfeeding if the mother is not already receiving antiretroviral treatment for her own health. FUNDING: Agence nationale de recherches sur le sida et les hépatites virales, Department for International Development, European and Developing Countries Clinical Trials Partnership, Thrasher Research Fund, Belgian Directorate General for International Cooperation, Centers for Disease Control and Prevention, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and UNDP/UNFPA/World Bank/WHO Special Programme of Research, Development and Research Training in Human Reproduction.