HIV Care & PMTCT in Resource-Limited Settings

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**Abstr.** Background: The use fixed-dose combination (FDC) is a critical tool in improving HAART. Studies on the effectiveness of combined lamivudine, stavudine and nevirapine (3TC/d4T/NVP) are scarce. Objective: To analyse 6861 patients in a large observational cohort from 21 Medecins Sans Frontieres (MSF) HIV/AIDS programmes taking 3TC/d4T/NVP, with subcohort analyses of patients at 12 and 18 months of treatment. Methods: Survival was analysed using Kaplan-Meier method and factors associated with progression to death with Cox proportional hazard ratio. Results: Median baseline CD4 count at initiating of FDC was 89 cells/µl [inter-quartile range (IQR), 33-158]. The median follow-up time was 4.1 months (IQR, 1.9-7.3). The incidence rate of death during follow-up was 14.2/100 person-years [95% confidence interval (CI), 13.8-14.5]. Estimates of survival (excluding those lost to follow-up) were 0.93 (95%CI, 0.92-0.94) at 6 months (n = 2,231) and 0.90 (95%CI, 0.89-0.91) at 12 months (n = 472). Using a Cox model, the following factors were associated with death: male gender, symptomatic infection, body mass index < 18 kg/m(2) and CD4 cell count 15-50 cells/µl or < 15 cells/µl. Subcohort analysis of 655 patients after 1 year of follow-up (M 2 FDC cohort) revealed that 77% remained on HAART, 91% of these still on the FDC regimen; 5% discontinued the FDC because of drug intolerance. At 18 months, 77% of the patients remained on HAART. Conclusions: Positive outcomes for d4T/3TC/NVP are reported for up to 18 months in terms of efficacy and safety.

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**Abstr.** Background: Structured treatment interruptions of highly-active antiretroviral therapy (HAART) might be particularly relevant for sub-Saharan Africa, where cost-saving strategies could help to increase the number of patients on HAART. We did a randomised trial of structured treatment interruption in Abidjan, Cote d’Ivoire. Methods: HIV-infected adults were randomised to receive continuous HAART (CT), CD4-guided HAART (CD4GT) with interruption and reintroduction thresholds at 350 and 250 cells per mm(3), respectively, or 2 months-off, 4-months-on HAART. Primary endpoints were death and severe morbidity (any WHO stage 3 or 4 events and any events leading to death) at month 24. We report data from the CT and CD4GT groups until Oct 31, 2005, when the data safety monitoring board recommended to prematurely stop the CD4GT arm. Analyses were intention-to-treat. This study is registered at ClinicalTrials.gov, number NCT00158405. Results: 326 adults (median CD4 count nadir 272 per mm(3)) were randomised to the CT or CD4GT groups and followed up for median of 20 months. Incidence of mortality (per 100 person-years) was not different between groups (CT 0.6, CD4GT 1.2; p=0.57). Incidence of severe morbidity (per 100 person-years) was higher in the CD4GT group (17.6) than in the CT group (6.7; p=0.001). The most frequent severe events were invasive bacterial diseases. 79% of severe morbidity episodes occurred in patients with CD4 count 200-500 per mm(3). Conclusion: Patients on CD4GT had severe morbidity rates 2.5-fold higher than those on CT. This difference was mainly due to high rates of common diseases in patients with CD4 count 200-500 per mm(3). This CD4-guided structured treatment interruption strategy should not be recommended in Abidjan.

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**Introduction.** It has been about 10 years since the first report that three drug combination antiretroviral therapy can durably suppress HIV replication.1 Subsequent studies have confirmed that when used appropriately highly active antiretroviral therapy (see box 1) can suppress viral replication to such low levels that the virus is unable to generate drug resistance mutations. Theoretically, once this level of viral suppression is achieved, treatment should work indefinitely, and the long term risk of morbidity and mortality related to HIV associated immunodeficiency becomes negligible. Experience to date suggests that lifelong suppression of HIV is feasible. This review is aimed at informing clinicians about the current management of HIV infection. Authoritative and continuously updated reviews are available on the web (for example, the US Department of Health and Human Services treatment guidelines at www.hivatis.org); this review does not attempt to exhaustively summarise the literature or to provide guidance to clinicians . . .

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Abstr. Context Combination anti-retroviral therapy or highly active antiretroviral therapy (HAART) has resulted in a dramatic decline in the incidence of opportunistic and other infections in human immunodeficiency virus (HIV)-infected adults and children. Objectives To estimate the incidence of 29 targeted opportunistic and other infections occurring in the era of HAART between January 1, 2001, and December 31, 2004, in HIV-infected infants, children, and adolescents followed up in Pediatric AIDS Clinical Trials Group (PACTG) 219C; to compare incidence rates in the HAART era to those of the pre-HAART era; and to test for linear trends over time in the HAART era. Design, Setting, and Participants Ongoing, multicenter, prospective cohort study designed to examine long-term outcomes in HIV-infected children. The study population included 2767 children enrolled between September 15, 2000, and December 31, 2004, with information entered in the database up to August 1, 2005, when data analysis was conducted. The pre-HAART era comparison population included 3331 children enrolled in 13 PACTG protocols from October 1988 to August 1998. Main Outcome Measures First occurrence of each of the 29 targeted infections. Results Seventy-five percent of the children were enrolled in the study and were followed for a median of 46 months (interquartile range: 32-57 months) after HAART initiation. At baseline, 5% were antiretroviral therapy (ART) non-naive, 39 and 55% were respectively at CDC stage B and C, median age, CD4 cell count and viral load were 37 years, 128 cells/μl and 5.2 log cp/ml, respectively. Ninety-three patients died during follow-up and the overall incidence rate of death was 6.3/100 person-years [95% confidence interval (CI), 5.2-7.7]. During the first year after HAART initiation, 47 patients died and seven were lost to follow-up, yielding to a probability of dying of 11.7% (95% CI, 8.9-15.3%). The death rate, which was highest during the first year after HAART initiation, decreased with time yielding a cumulative probability of dying of 17.4% (95% CI, 13.9-21.5%) and 24.6% (95% CI, 20.4-29.4%) at 2 and 5 years. Causes of death were ascertained in 76 deaths. Mycobacterial infections, neurotropic infections and septicemia were the most frequent likely causes of death. Conclusions: This study underlines the early mortality pattern after HAART initiation and highlights the leading role of mycobacterial infections in the causes of death.

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Tuberculosis (TB) is the preeminent manifestation of HIV infection and has become a leading cause of maternal mortality and morbidity in high HIV prevalence settings. Active TB in pregnant women has potentially serious consequences for fetuses and newborns. In Soweto, South Africa, there is a more than 90% uptake of voluntary counseling and HIV testing during routine antenatal care, and almost one third of pregnant women are HIV-infected. The posttest counseling session of the prevention of mother-to-child transmission program provides an opportunity to screen HIV-infected pregnant women for TB. III this Study, 370 HIV-infected pregnant women were screened for symptoms of active TB by lay counselors at the posttest counseling session. If symptomatic, they were referred to nurses who investigated them further. Eight women were found to have previously undiagnosed, smear-negative, culture-confirmed T13 (2160/100 000). The mean CD4 count in those with active TB compared to those without TB was 276 x 10(6) cells per liter vs 447 x 10(6) cells per liter (P = 0.051). Symptoms most associated with active Tb were hemoptysis and fever. We conclude that rates of Tb in HIV-infected pregnant women are high, and screening for TB during routine antenatal care should be implemented in high HIV prevalence settings.

Abstr. Seventy human immunodeficiency virus ( HIV) -infected patients receiving rifampicin and 70 HIV-infected patients not receiving rifampicin were enrolled to receive 400 mg of nevirapine-based highly active antiretroviral therapy per day. Mean plasma nevirapine levels at 8 and 12 weeks were lower in patients receiving rifampicin (P = .048). However, viro. 048 logical and immunological outcomes at 24 weeks were not different between the 2 groups (P > .05).

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additional years of survival benefit. Conclusions. At least 3.0 million years of life have been saved in the United States as a direct result of care of patients with AIDS, highlighting the significant advances made in HIV disease treatment.

See the editorial commentary by Vermund.

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Abstr. Background: Cotrimoxazole is recommended for prevention of opportunistic infections in symptomatic HIV patients in sub-Saharan Africa. Methods: We examined the feasibility and effectiveness of daily cotrimoxazole prophylaxis in a well-established cohort of HIV-infected adults attending clinics in Entebbe, Uganda. We compared mortality and morbidity rates for 12 months before and after the introduction of cotrimoxazole. Results: Between August 2000 and February 2002, 94% of cohort members were enrolled onto cotrimoxazole prophylaxis. Revisits were scheduled every 4 weeks to replenish pills; patients attended 61% of revisits. The main reasons for nonenrollment and defaulting were lack of transport, being away from home, and sickness. Drug-related adverse events, mainly itching and rash, were seen in 4% of participants. Although bacterial resistance rate to cotrimoxazole was high, the adjusted mortality incidence rate ratio was significantly reduced after the introduction of cotrimoxazole (0.76; 95% confidence interval, 0.60-0.96; P = 0.020). Overall febrile events and morbidity rates were unchanged after the introduction of cotrimoxazole, but the incidence of malaria was reduced (incidence rate ratio, 0.31; 95% confidence interval, 0.13-0.72). Conclusions: Cotrimoxazole prophylaxis can be introduced into routine HIV clinic activities and is associated with a reduction in overall mortality and malaria morbidity, even in all area with high bacterial resistance. These results reinforce the need for large-scale provision of cotrimoxazole prophylaxis for all HIV-positive patients in developing countries.

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