



WHO, Reproductive Health and Research

HIV Care & PMTCT in Resource-Limited Settings

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prepared by the Bordeaux Working Group

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Number of citations selected for this issue: 6

Citation format (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr.** (Authors' abstract) or **Notes** (prepared by the Bordeaux Working Group) **Author address**, if available, **Subject Headings**

Subject headings / Subheadings indexing the selected references (by alphabetical order)

Adults / Women	Eastern Europe	Infant feeding / Breastfeeding	Prevention of Mother-To-Child Transmission (PMTCT) / AntiRetroViral (ARV)	Treatment impact and response
Children	Gynæcology	Infections (Others) / Prophylaxis	Prevention of sexual transmission	Treatment monitoring
Clinical manifestations (Others)	Hepatitis B infection (HBV)	Low Income Countries (LICs) / Africa, Asia, Carribean, South America	Randomized Controlled Trial (RCT)	Treatment programme
Comprehensive care	Hepatitis C infection (HCV)	Mother-To-Child Transmission (MTCT)	Termination of pregnancy / Abortion	Tuberculosis (TB) / Prophylaxis
Conference summary	Highly Active AntiRetroviral Treatment (HAART)	Natural history	Treatment adherence	Viral resistance
Contraception	Industrialized countries	Obstetrics	Treatment complications	Voluntary Counselling and Testing (VCT)

Bourgeois A, Laurent C, Mougnotou R, Nkoue N, Lactuock B, Ciaffi L, Liegeois F, Andrieux Meyer I, Zekeng L, Calmy A, Mpoudi Ngole E, Delaporte E. **Field assessment of generic antiretroviral drugs: a prospective cohort study in Cameroon.** *Antiviral Therapy* 2005;10(2):335-341.

Abstr. Objective: To assess the effectiveness of generic antiretroviral drugs in terms of survival and virological and immunological responses, as well as their tolerability and the emergence of viral resistance. Methods: A total of 109 HIV-1-infected patients were enrolled in a prospective cohort study in Yaounde, Cameroon. Available generic drugs were a fixed-dose combination (FDC) of zidovudine (ZDV) and lamivudine (3TC), an FDC of 3TC, stavudine (d4T) and nevirapine (NVP), and individual formulations of ZDV, 3TC and NVP. Results: At baseline, the median CD4 cell count was 150/mm³ [interquartile range (IQR) 61-223] and median viral load was 5.4 log₁₀ copies/ml [IQR 4.8-5.6]; 78% of patients received ZDV/3TC/NVP and 22% received 3TC/d4T/NVP. Median follow-up was 16 months (IQR 11-23). The survival probability was high (0.92 at 12 months); plasma viral load declined by a median of 3.3 log₁₀ copies/ml and 86.9% of the intention-to-treat population had viral load < 400 copies/ml at 12 months; CD4 count had increased by a median of 106 cells/mm³ at 12 months; drug resistance rarely emerged (incidence rate 3.2 per 100 person-years); and the treatments were reasonably well-tolerated (incidence rate of severe adverse effects 7.8 per 100 person-years). Conclusion: Together with previous pharmacological and clinical studies, this prospective study suggests that these generic antiretroviral drugs can be used in developing countries.

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Adults, HAART, LICs / Africa, Treatment impact and response

Boyd M, Mootsikapun P, Burger D, Chuenyam T, Ubolyam S, MahAnontharit A, Sangkote J, Bunyaprawit P, Horsakulchai M, Lange J, Cooper D, Phanuphak P, Ruxrungtham K. **Pharmacokinetics of reduced-dose indinavir/ritonavir 400/100 mg twice daily in HIV-1-infected Thai patients.** *Antiviral Therapy* 2005;10(2):301-307.

Abstr. Objective: To study the pharmacokinetics of indinavir/ ritonavir 400/100 mg twice daily in antiretroviral-naïve patients at Srinagarind Hospital in Khon Kaen, Thailand. Methods: This was a steady-state, open-label pharmacokinetic study of 19 patients. A 12 h pharmacokinetic curve was recorded after an overnight fast. Plasma levels of indinavir and ritonavir were determined by a validated HPLC method. Virological failure was defined according to the most recent US Department of Health and Human Services guidelines as a viral load above 400 copies/ml at week 24. Results: Median baseline values for CD4 and viral load were 13cells/mm³ and 167000copies/ml, respectively. The median (interquartile ranges) for indinavir AUC, C-max and C-min, were 18.1 (15.3-23.8) mg/l center dot h, 4.1 (3.6-4.8) mg/l and 0.17 (0.12-0.30)mg/l, respectively. These values represent 37%, 39% and 24% of the AUC, C-max and C-min values found, respectively, for the indinavir/ritonavir 800/100 mg dose in HIV-1-infected Thai patients. Shortterm virological response was satisfactory. There were three subjects with an indinavir C-min below the target value of 0.10mg/l, of whom one had virological failure (33%). Among the other 16 subjects with an indinavir C-min above 0.10mg/l, there was also one virological failure (6%) (P=0.30). Conclusions: Indinavir exposure in this reduced-dose regimen of 400 mg with 100 mg ritonavir twice daily was more than dose-proportionally lower than previously observed with the indinavir/ritonavir 800/100 mg twice daily regimen. Therapeutic Cmin levels of indinavir were achieved in > 80% of the subjects and short-term virological response was satisfactory in this cohort of patients starting highly active antiretroviral therapy at an advanced disease stage with high baseline viral loads.

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Adults, HAART, LICs / Asia, Treatment impact and response, Treatment monitoring

Gray RH, Li XB, Kigozi G, Serwadda D, Brahmbhatt H, Wabwire Mangen F, Nalugoda F, Kiddugavu M, Sewankambo N, Quinn TC, Reynolds SJ, Wawer MJ. **Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study.** *Lancet* 2005;366(9492):1182-1188.

Abstr. Background HIV acquisition is significantly higher during pregnancy than in the postpartum period. We did a prospective study to estimate HIV incidence rates during pregnancy and lactation. Methods We assessed 2188 HIV-negative sexually active women with 2625 exposure intervals during pregnancy and 2887 intervals during breastfeeding, and 8473 non-pregnant and non-lactating women with 24 258 exposure intervals. Outcomes were HIV incidence rates per 100 person years and incidence rate ratios estimated by Poisson multivariate regression, with the non-pregnant or non-lactating women as the reference group. We also assessed the husbands of the married women to study male risk behaviours. Findings HIV incidence rates were 2.3 per 100 person years during pregnancy, 1.3 per 100 person years during breastfeeding, and 1.1 per 100 person years in the non-pregnant and non-lactating women. The adjusted incidence rate ratios were 2.16 (95% CI 1.39-3.37) during pregnancy and 1.16 (0.82-1.63) during breastfeeding. Pregnant women and their male partners reported significantly fewer external sexual partners than did the other groups. In married pregnant women who had a sexual relationship with their male spouses, the HIV incidence rate ratio was 1.36 (0.63-2.93). In married pregnant women in HIV-discordant relationships (ie, with HIV-positive men) the incidence rate ratio was 1.76

(0.62-4.03). Interpretation The risk of HIV acquisition rises during pregnancy. This change is unlikely to be due to sexual risk behaviours, but might be attributable to hormonal changes affecting the genital tract mucosa or immune responses. HIV prevention efforts are needed during pregnancy to protect mothers and their infants.

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LICs / Africa, MTCT

McIntyre JA. **Sex, pregnancy, hormones, and HIV** [Comment]. *Lancet* 2005;366(9492):1141-1142.

Introduction: In today's *Lancet*, Ron Gray and colleagues report an increased risk of incident HIV during pregnancy in Uganda. They draw on the unique research situation in Rakai to provide information on an important topic: does pregnancy increase the risk of HIV infection for women, and, if so, is this effect due to biology or behaviour? The results show a doubling in the risk of HIV acquisition during pregnancy—an HIV incidence of 2.3 per 100 person-years during pregnancy, compared with 1.3 per 100 person-years during lactation and 1.1 per 100 person-years in women who were not pregnant or lactating. Other investigators have reported high rates of HIV seroconversion in pregnancy, and but the large number of women studied, the ability to follow them up through pregnancy and lactation, and the information on male and female sexual behaviour add to the strength of the Rakai study. The authors have been able to control for sexual behaviour to a greater extent than previous reports, and they show little effect of behavioural factors on the increased risk of HIV acquisition in pregnant women, suggesting that biological changes in pregnancy have an important role.

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LICs / Africa, MTCT

Michailidis C, Pozniak AL, Mandalia S, Basnayake S, Nelson MR, Gazzard BG. **Clinical characteristics of IRIS syndrome in patients with HIV and tuberculosis.** *Antiviral Therapy* 2005;10(3):417-422.

Abstr. Background: Some patients with HIV/tuberculosis (TB) coinfection who are on anti-TB treatment and highly active antiretroviral therapy (HAART) will develop an exacerbation of symptoms, signs or radiological manifestations of TB that are not due to relapse or recurrence of their TB. The aetiology of these immune reconstitution inflammatory syndrome (IRIS) reactions is unknown but it is presumed that they occur, at least in part, as a consequence of HAART-related reconstitution of immunity. Methods: Patients who were diagnosed with their first episode of definitive or presumed TB between January 2001 and July 2003 were identified from the Chelsea and Westminster TB/HIV database. The patients were classified into those who developed IRIS and those who did not using a set definition of the syndrome. Demographic, clinical and laboratory data relating to both HIV and TB were compared between the two groups. Results: A total of 55 cases of TB were identified, of which 45 cases were confirmed on culture or gene probe and 10 were presumed cases. Fourteen cases (25.5%) developed IRIS with a median (range) duration of 2.53 (0.53-14.97) months. The median baseline CD4 [interquartile range (IQR)] for the IRIS group was significantly lower at 80 (33-117) cells/mm³ (P=0.05) than the non-IRIS group at 139 (77-284) cells/mm³. A significantly greater proportion of patients in the IRIS group (11/14 (78.6%). P=0.011] had baseline CD4 < 100cells/mm³ compared with the non-IRIS group [16/41 (39.0%)]. There was no significant difference between the two groups when comparing the log (10) baseline viral load (VL). Eight (57.0%) patients in the IRIS group had disseminated TB at baseline compared with seven (17.0%) in the non-IRIS group (P=0.006). In those who had a detectable VL at baseline, the median fold change (1013) in CD4 from baseline to 3 months was significantly higher in the IRIS group patients, 1.5 (0.6-5.6), compared with 0.7 (-0.2 to 1.0) for those in the non-IRIS group (P=0.046). Conclusions: Patients who develop IRIS are more likely to present with disseminated TB, have a CD4 count < 100 cells/mm³ and have a prompt rise in CD4 count in the initial 3 months of HAART.

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HAART, Industrialized countries, Infections (Others) / Prophylaxis, Tuberculosis (TB)

Moh R, Danel C, Sorho S, Sauvageot D, Anzian A, Minga A, Gomis OB, Kanga C, Inwoley A, Gabillard D, Bissagnene E, Salamon R, Anglaret X. **Haematological changes in adults receiving a zidovudine-containing HAART regimen in combination with cotrimoxazole in Cote d'Ivoire.** *Antiviral Therapy* 2005;10(5):615-624.

Abstr. Objective: Neutropenia is the most frequent side effect of cotrimoxazole in sub-Saharan Africa. We estimated the incidence of haematological disorders during the first 6 months of a zidovudine-containing highly active antiretroviral therapy (HAART) regimen in sub-Saharan African adults receiving cotrimoxazole. Methods: Prospective cohort study in Abidjan, with blood cell count measurement at baseline (HAART initiation), month 1, month 3 and month 6. Results: A total of 498 adults [baseline: 80% currently on cotrimoxazole prophylaxis; median CD4 count 237/mm³ [interquartile range (IQR) 181;316]; median neutrophil count 1647/mm³ (IQR 1221;2256); median haemoglobin 113 g/l (IQR 102;122)] started zidovudine (AZT) lamivudine/efavirenz. During follow-up, 118 patients had a grade 3-4 neutropenia [(56.3/100 person-years (PY)], 23 had a grade 3-4 anaemia (9.6/100PY) and no cases of grade 3-4 thrombocytopenia. Of the 118 patients with grade 3-4 neutropenia, 86 (73%) had to stop cotrimoxazole because neutropenia persisted, and one (< 1%) had to stop AZT because of persistent neutropenia after cotrimoxazole was stopped (neutropenia-related HAART modification: 0.4/100 PY). Of the 23 patients with grade 3-4 anaemia, 11 had to stop AZT (anaemia-related HAART modification: 4.4/100 PY). In patients who stopped cotrimoxazole but not AZT, the median gain in neutrophils at 1 month was +540/mm³ (IQR +150;+896). Conclusions: At baseline, most patients had a normal neutrophil count and 80% of them were already receiving cotrimoxazole. An unexpectedly high rate of grade 3-4 neutropenia occurred shortly after introduction of AZT. Almost all of the persistent severe neutropenia disappeared after cotrimoxazole was stopped. This suggests an accentuated drug interaction between the two drugs in these sub-Saharan African individuals. Grade 3-4 anaemia was much less frequent, but remained the first cause of AZT discontinuation.

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HAART, LICs / Africa, Treatment complications