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## HIV Care & PMTCT in Resource-Limited Settings

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prepared by the Bordeaux Working Group

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**Citation format** (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr.** (Authors' text) or **Introduction** (Authors' text) or **Selection** (Selected sections of the paper) or **Notes** (Written by the Bordeaux Working Group). **Author Address**, if available, **Free Full Text**, if available

Calmy A, Hirschel B, Cooper DA, Carr A. **Clinical update: adverse effects of antiretroviral therapy**. *Lancet* 2007;370(9581):12-14.

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Chi BH, Chintu N, Lee A, Stringer EM, Sinkala M, Stringer JSA. **Expanded services for the prevention of mother-to-child HIV transmission - Field acceptability of a pilot program in Lusaka, Zambia**. *Journal of Acquired Immune Deficiency Syndromes* 2007;45(1):125-127.

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Chi BH, Sinkala M, Stringer EM, Cantrell RA, Mtonga V, Bulterys M, Zulu I, Kankasa C, Wilfert C, Weidle PJ, Vermund SH, Stringer JSA. **Early clinical and immune response to NNRTI-based antiretroviral therapy among women with prior exposure to single-dose nevirapine**. *AIDS* 2007;21(8):957-964.

**Abstr.** Objective: To determine whether prior exposure to single-dose nevirapine (NVP) for prevention of mother-to-child HIV transmission (PMTCT) is associated with attenuated CD4 cell response, death, or clinical treatment failure in women starting antiretroviral therapy (ART) containing non-nucleoside reverse transcriptase inhibitors (NNRTI). Methods: Open cohort evaluation of outcomes for women in program sites across Zambia. HIV treatment was provided according to Zambian/World Health Organization guidelines. Results: Peripartum NVP exposure status was known for 6740 women initiating NNRTI-containing ART, of whom 751 (11%) reported prior use of NVP for PMTCT. There was no significant difference in mean CD4 cell change between those exposed or unexposed to NVP at 6 (+202 versus +182 cells/ $\mu$ l;  $P=0.20$ ) or 12 (+201 versus +211 cells/ $\mu$ l;  $P=0.60$ ) months. Multivariable analyses showed no significant differences in mortality [adjusted hazard ratio (HR), 1.2; 95% confidence interval (CI), 0.8-1.8] or clinical treatment failure (adjusted HR, 1.1; 95% CI, 0.8-1.5). Comparison of recent NVP exposure with remote exposure suggested a less favorable CD4 cell response at 6 (+150 versus +219 cells/ $\mu$ l;  $P=0.06$ ) and 12 (+149 versus +215 cells/ $\mu$ l;  $P=0.39$ ) months. Women with recent NVP exposure also had a trend towards elevated risk for clinical treatment failure (adjusted HR, 1.6; 95% CI, 0.9-2.7). Conclusion: Exposure to maternal single-dose NVP was not associated with substantially different short-term treatment outcomes. However, evidence was suggestive that exposure within 6 months of ART initiation may be a risk factor for poor treatment outcomes, highlighting the importance of ART screening and initiation early in pregnancy.

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Creek TL, Ntumy R, Seipone K, Smith M, Mogodi M, Smit M, Legwaila K, Molokwane I, Tebele G, Mazhani L, Shaffer N, Kilmarx PH. **Successful introduction of routine opt-out HIV testing in antenatal care in Botswana**. *Journal of Acquired Immune Deficiency Syndromes* 2007;45(1):102-107.

**Abstr.** Background: Botswana has high HIV prevalence among pregnant women (37.4% in 2003) and provides free services for prevention of mother-to-child transmission (PMTCT) of HIV. Nearly all pregnant women (> 95%) have antenatal care (ANC) and deliver in hospital. Uptake of antenatal HIV testing was low from 1999 through 2003. In 2004, Botswana's President declared that HIV testing should be "routine but not compulsory" in medical settings. Methods: Health workers were trained to provide group education and recommend HIV testing as part of routine ANC services. Logbook data on ANC attendance, HIV testing, and uptake of PMTCT interventions were reviewed before and after routine testing training, and ANC clients were interviewed. Results: After routine testing started, the percentage of all HIV-infected women delivering in the regional hospital who knew their HIV status increased from 47% to 78% and the percentage receiving PMTCT interventions increased from 29% to 56%. ANC attendance and the percentage of HIV-positive women who disclosed their HIV status to others remained stable. Interviews indicated that ANC clients supported the policy. Conclusions: Routine HIV testing was more accepted than voluntary testing in this setting and led to

substantial increases in the uptake of testing and PMTCT interventions without detectable adverse consequences. Routine testing in other settings may strengthen HIV care and prevention efforts.

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European Collaborative Study. **Time to undetectable viral load after highly active antiretroviral therapy initiation among HIV-infected pregnant women.** *Clinical Infectious Diseases* 2007; 44(12):1647-1656.

**Abstr.** Background. There have been no clinical trials in resource-rich regions that have addressed the question of which highly active antiretroviral therapy (HAART) regimens are more effective for optimal viral response in antiretroviral-naive, human immunodeficiency virus (HIV)-infected pregnant women. Methods. Data on 240 HIV-1-infected women starting HAART during pregnancy who were enrolled in the prospective European Collaborative Study from 1997 through 2004 were analyzed. An interval-censored survival model was used to assess whether factors, including type of HAART regimen, race, region of birth, and baseline immunological and virological status, were associated with the duration of time necessary to suppress viral load below undetectable levels before delivery of a newborn. Results. Protease inhibitor-based HAART was initiated in 156 women (65%), 125 (80%) of whom received nelfinavir, and a nevirapine-based regimen was initiated in the remaining 84 women (35%). Undetectable viral loads were achieved by 73% of the women by the time of delivery. Relative hazards of time to achieving viral suppression were 1.54 (95% confidence interval, 1.05-2.26) for nevirapine-based HAART versus PI-based regimens and 1.90 (95% confidence interval, 1.16-3.12) for western African versus non-African women. The median duration of time from HAART initiation to achievement of an undetectable viral load was estimated to be 1.4 times greater in women receiving PI-based HAART, compared with women receiving nevirapine-based HAART. Baseline HIV RNA load was also a significant predictor of the rapidity of achieving viral suppression by delivery, but baseline immune status was not. Conclusions. In this study, nevirapine-based HAART (compared with PI [mainly nelfinavir]-based HAART), western African origin, and lower baseline viral load were associated with shorter time to achieving viral suppression.

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Feiterna Sperling C, Weizsaecker K, Buhrer C, Casteleyn S, Loui A, Schmitz T, Wahn V, Obladen M. **Hematologic effects of maternal antiretroviral therapy and transmission prophylaxis in HIV-1-exposed uninfected newborn infants.** *Journal of Acquired Immune Deficiency Syndromes* 2007; 45(1):43-51.

**Abstr.** Objective: A prospective observational study to investigate hematologic alterations during the first 3 months of life in HIV-exposed uninfected infants subjected to antiretroviral medication before and after birth. Methods: Two hundred twenty-one consecutive uninfected infants born to HIV-positive mothers on antiretroviral medication during pregnancy were included. Perinatal transmission prophylaxis comprised zidovudine (ZDV) administered intravenously intrapartum and 10 days after birth. Blood counts and differentials were determined at birth and at 2, 4, 6, and 12 weeks of age, and hematologic toxicity was graded according to pediatric toxicity scales. Data were analyzed according to the kind of prenatal medication (ZDV alone or with another nucleoside reverse transcriptase inhibitor [NRTI] vs. highly active antiretroviral therapy [HAART]). Results: Median hemoglobin was significantly lower in HAART-exposed newborns from birth ( $P = 0.004$ ) until day 28. During follow-up, 119 (53.8%) infants had anemia grade 2 or higher on at least 1 occasion; 16 (7.2%) received red blood cell transfusion at 23 (range: 1-56) days of age. Neutropenia grade 2 or higher occurred in 106 (48.0%) infants at least once, 8 infants had staphylococcal infections, and 2 infections were severe. After adjustment for possible confounders (prematurity, birth weight, ethnicity, gender, duration of maternal antiretroviral therapy, maternal Centers for Disease Control and Prevention stage, and maternal illicit drug use), HAART exposure

was the only independent risk factor for anemia (odds ratio [OR] 2.22, 95% confidence interval [CI]: 1.06 to 4.64;  $P = 0.034$ ) and neutropenia (OR = 2.15 CI: 1.02 to 4.55;  $P = 0.045$ ). Conclusions: Antiretroviral transmission prophylaxis is associated with significant anemia and neutropenia in HIV-uninfected infants during the first 3 months of life. Anemia was more profound in HAART-exposed infants.

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Hirschel B, Perneger T. **No patient left behind - better treatments for resistant HIV infection.** *Lancet* 2007;370(9581):3-5.

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Lazzarin A, Campbell T, Clotet B, Johnson M, Katlama C, Moll A, Towner W, Trortier B, Peeters M, Vingerhoets J, de Smedt G, Baeten B, Beets G, Sinha R, Woodfall B. **Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-2: 24-week results from a randomised, double-blind, placebo-controlled trial.** *Lancet* 2007;370(9581):39-48.

**Abstr.** Background TMC125 (etravirine) is a non-nucleoside reverse-transcriptase inhibitor (NNRTI) with activity against NNRTI-resistant HfV-1 in phase IIb trials. The aim of DUET-2 is to examine the efficacy, tolerability, and safety of TMC125 in treatment-experienced patients. Methods In this continuing randomised, double-blind, placebo-controlled, phase III trial, HIV-1-infected patients on failing antiretroviral therapy with evidence of resistance to currently available NNRTIs and at least three primary protease inhibitor mutations were eligible for enrolment if on stable (8 weeks unchanged) antiretroviral therapy with plasma HIV-1 RNA greater than 5000 copies per mL. Patients were randomly assigned to receive either TMC125 (200 mg) or placebo, each given twice daily with darunavir-ritonavir, investigator-selected nucleoside/nucleotide reverse transcriptase inhibitors, and optional enfuvirtide. The primary endpoint was the proportion of patients with confirmed viral load below 50 copies per mL at week 24 (FDA time-to-loss of virological response algorithm). Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00255099. Findings 591 patients were randomised and treated (295 patients in the TMC125 group and 296 in the placebo group). By week 24, 51 (17%) patients in the TMC125 group and 73 (25%) in the placebo group had discontinued, mainly because of virological failure. 183 (62%) patients in the TMC125 group and 129 (44%) in the placebo group achieved confirmed viral load below 50 copies per mL at week 24 (difference 18%, 95% CI 11-26;  $p = 0.0003$ ). The type and frequency of adverse events were: much the same in the two groups. Interpretation In treatment-experienced patients, treatment with TMC125 led to better virological suppression at week 24 than did placebo. The safety and tolerability profile of TMC125 was generally comparable with placebo.

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Lopez Gatell H, Cole SR, Hessel NA, French AL, Greenblatt RM, Landesman S, Preston Martin S, Anastos K. **Effect of tuberculosis on the survival of women infected with human immunodeficiency virus.** *American Journal of Epidemiology* 2007;165(10):1134-1142.

**Abstr.** Evidence regarding the effect of tuberculosis (TB) disease on progression of human immunodeficiency virus (HIV) disease is inconclusive. The authors estimated the effect of time-varying incident TB on time to acquired immunodeficiency syndrome (AIDS)-related mortality using a joint marginal structural Cox model. Between 1995 and 2002, 1,412 HIV type 1 (HIV-1)-infected women enrolled in the Women's Interagency HIV Study were followed for a median of 6 years. Twenty-nine women incurred incident TB, and 222 died of AIDS-related causes. Accounting for age, CD4 cell count, HIV-1 RNA level, serum albumin level, and non-TB AIDS at study entry, as well as for time-varying CD4 cell count, CD4 cell count nadir, HIV-1 RNA level, peak HIV-1 RNA level, serum

albumin level, HIV-related symptoms, non-TB AIDS, anti-Pneumocystis jiroveci prophylaxis, antiretroviral therapy, and household income, the hazard ratio for AIDS-related death comparing time after incident TB with time before incident TB was 4.0 (95% confidence interval (CI): 1.2, 14). The effect of incident TB on mortality was similar among highly active antiretroviral therapy (HAART)-exposed women (hazard ratio = 4.3, 95% CI: 0.9, 22) and non-HAART-exposed women (hazard ratio = 3.9, 95% CI: 0.9, 17; interaction  $p = 0.91$ ). Although results were imprecise because few women incurred TB, irrespective of HAART exposure, incident TB increases the hazard of AIDS-related death among HIV-infected women.

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Madruga JV, Berger D, McMurchie M, Suter F, Banhegyi D, Ruxrungtham K, Norris D, Lefebvre E, de Bethune MP, Tomaka F, De Pauw M, Vangeneugden T, Spinoso Guzman S. **Efficacy and safety of darunavir-ritonavir compared with that of lopinavir-ritonavir at 48 weeks in treatment-experienced, HIV-infected patients in TITAN: a randomised controlled phase III trial.** *Lancet* 2007;370(9581):49-58.

**Abstr.** Background The protease inhibitor darunavir has been shown to be efficacious in highly treatment-experienced patients with HIV infection, but needs to be assessed in patients with a broader range of treatment experience. We did a randomised, controlled, phase III trial (TITAN) to compare 48-week efficacy and safety of darunavir-ritonavir with that of lopinavir-ritonavir in treatment-experienced, lopinavir-naive patients. Methods Patients received optimised background regimen plus non-blinded treatment with darunavir-ritonavir 600/100 mg twice daily or lopinavir-ritonavir 400/100 mg twice daily. The primary endpoint was non-inferiority (95% CI lower limit for the difference in treatment response  $\geq 12\%$  or greater) for HIV RNA of less than 400 copies per mL in plasma at week 48 (per-protocol analysis). TITAN (TMC114-C214) is registered with ClinicalTrials.gov, number NCT00110877. Findings Of 595 patients randomised and treated, 187 (31%) were protease inhibitor naive; 476 of 582 (82%) were susceptible to four or more protease inhibitors. At week 48, significantly more darunavir-ritonavir than lopinavir-ritonavir patients had HIV RNA of less than 400 copies per mL (77% [220 of 286] vs 68% [199 of 293]; estimated difference 9%, 95% CI 2-16). Fewer virological failures treated with darunavir-ritonavir than with lopinavir-ritonavir developed primary protease inhibitor mutations (21% [ $n = 6$ ] vs 36% [ $n = 20$ ]) and nucleoside analogue-associated mutations (14% [ $n = 4$ ] vs 27% [ $n = 15$ ]). Safety data were generally similar between the groups; grade 3 or 4 adverse events occurred in 80 (27%) darunavir-ritonavir and 89 (30%) lopinavir-ritonavir patients. Interpretation In lopinavir-naive, treatment-experienced patients, darunavir-ritonavir was non-inferior to lopinavir-ritonavir treatment in terms of our virological endpoint, and should therefore be considered as a treatment option for this population.

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Madruga JV, Cahn P, Grinsztejn B, Haubrich R, Lalezari J, Mills A, Pialoux G, Wilkin T, Peeters M, Vingerhoets J, de Smedt G, Leopold L, Trefiglio R, Woodfall B. **Efficacy and safety of TMC125 (etravirine) in treatment-experienced HIV-1-infected patients in DUET-1: 24-week results from a randomised, double-blind, placebo-controlled trial.** *Lancet* 2007;370(9581):29-38.

**Abstr.** Background Antiretroviral agent; active against drug-resistant HIV-1 are needed for treatment-experienced patients. The aim of this trial was to assess the efficacy, safety; and tolerability of TMC125 (etravirine), a non-nucleoside reverse transcriptase inhibitor (NNRTI). Methods DUET-1 is a continuing, multinational randomised, double-blind, placebo-controlled, phase III trial. Treatment-experienced adult patients with virological failure on stable antiretroviral therapy, documented genotypic evidence of NNRTI resistance, Aral load over 5000 copies per mL, and three or more primary protease inhibitor mutations were randomly assigned to receive 200 mg TMC125 or placebo twice daily. All patients also received darunavir with low-dose ritonavir and

investigator-selected nucleoside reverse transcriptase inhibitors. Enfuvirtide use was optional. The primary endpoint was a confirmed viral load below 50 copies per mL at week 24 (FDA time-to-loss of virological response algorithm). Analyses were done by intention to treat. This trial is registered with ClinicalTrials.gov, with the number NCT00254046. Findings 612 patients were randomised and treated (304 in the TMC125 group, 308 in the placebo group). By week 24, 42 (14%) patients in the TMC125 group and 56 (18%) in the placebo group had discontinued, mainly due to virological failure. At week 24, 170 (56%) patients in the TMC125 group and 119 (39%) patients in the placebo group achieved a confirmed viral load of less than 50 copies per mL (difference in response rates 17%; 95% CI 9-25;  $p = 0.005$ ). Most adverse events were mild or moderate in severity. The type and incidence of adverse events, including neuropsychiatric events, seen with TMC125 were generally comparable with placebo, with the exception of rash (61 [20%] patients on TMC125 vs 30 [10%] on placebo) and diarrhoea (36 [12%] patients on TMC125 vs 63 [20%] on placebo). Interpretation In treatment-experienced patients with NNRTI resistance, treatment with TMC125 achieved better virological suppression at week 24 than did placebo. The safety and tolerability profile of TMC125 was generally comparable with placebo.

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Rangaka MX, Diwakar L, Seldon R, van Cutsem G, Meintjes GA, Morrioni C, Mouton P, Shey MS, Maartens G, Wilkinson KA, Wilkinson RJ. **Clinical, immunological, and epidemiological importance of antituberculosis T cell responses in HIV-infected Africans.** *Clinical Infectious Diseases* 2007;44(12):1639-1646.

**Abstr.** Background. Human immunodeficiency virus (HIV)-associated tuberculosis is a major cause of mortality in Africa. The assay of T cell interferon-gamma released in response to antigens of greater specificity than purified protein derivative is a useful improvement over the Mantoux tuberculin skin test, but few studies have evaluated interferon gamma secretion in HIV-infected individuals. Methods. Mycobacterium tuberculosis antigen-specific interferon-gamma secretion was assessed by whole blood assay and enzyme-linked immunospot, which were compared with the Mantoux tuberculin skin test in HIV-infected and HIV-uninfected individuals without active tuberculosis and HIV-infected patients with pulmonary tuberculosis in Khayelitsha, South Africa. Results. The skin test and whole blood assay responses to purified protein derivative in HIV-positive subjects were decreased, compared with responses in HIV-negative subjects ( $P < .001$ ). By contrast, the responses to M. tuberculosis antigens (early secreted antigenic target 6, culture filtrate protein 10, TB10.3, and alpha-crystallin 2) were less affected, indicating a high prevalence of latent tuberculosis (similar to 80%) in both HIV-negative and HIV-positive subject groups. Whole blood assay responses did not differ between the HIV-positive subjects without tuberculosis and HIV-positive subjects with tuberculosis, but the enzyme-linked immunospot method response to early secreted antigenic target 6 and culture filtrate protein 10 was higher in the group of HIV-infected subjects with tuberculosis ( $P \leq .04$ ), although this group had lower CD4(+) cell counts. A ratio of the combined enzyme-linked immunospot method response divided by the CD4(+) cell count of 11.0 had 88% sensitivity and 80% specificity for active pulmonary tuberculosis in HIV-infected individuals. Conclusions. Interferon-gamma release appears to be less impaired than skin testing by HIV coinfection. The novel potential to relate the enzyme-linked immunospot method and CD4(+) cell count to assist diagnosis of active tuberculosis in patients with HIV infection is important and deserves further evaluation.

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Tam LWY, Hogg RS, Yip B, Montaner JSG, Harrigan PR, Brumme CJ. **Performance of a World Health Organization first-line regimen (stavudine / lamivudine / nevirapine) in antiretroviral-naive individuals in a Western setting.** HIV Medicine 2007;8(5):267-270.

**Abstr.** Objectives In 2003, the World Health Organization (WHO) and Joint United Nations Programme on HIV/AIDS (UNAIDS) introduced the '3 by 5 Initiative' to treat 3 million individuals by the end of 2005. This study evaluates the time to treatment termination, viral load suppression, and detection of drug resistance among antiretroviral-naive individuals initiating stavudine/lamivudine/nevirapine (d4T/3TC/NVP) in British Columbia, Canada, to provide a context for future programme planning. Methods Primary outcome was time to treatment termination. Secondary outcome was time to viral suppression. Accumulation of drug resistance mutations was followed systematically in the first 145 individuals over 30 months. Cox proportional hazard regression identified factors associated with termination and suppression. Results 312 antiretroviral-naive individuals initiated d4T/3TC/NVP between August 1996 and September 2003. Median follow-up time was 26.5 months (interquartile range [IQR] 6.8-46.5). At a median of 12.4 months (IQR 4.3-33.3), 132 (42.3%) patients switched treatment, 53 (17.0%) stopped therapy and 26 (8.3%) died. Of 308 subjects with baseline viral load > 500 copies/mL, 223 (72.4%) suppressed to ≤ 500 copies/mL at a median of 2.0 months. Among 145 (46.5%) individuals followed longitudinally, resistance mutations to NNRTI, 3TC, or other NRTI were detected in 11 (7.6%), six (4.1%) and four (2.8%) individuals after 12 months of therapy; and in 23 (15.9%), 17 (12.0%), and six (4.1%) individuals after 30 months. Conclusions The population requiring second-line treatment was 30% at 12 months and 40% at 24 months; 20% had detectable drug resistance mutations by 30 months. While these results are from a Western setting, they illustrate the need to consider second- and third-line approaches as antiretroviral treatment scale-up continues in the developing world.

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Townsend CL, Cortina Borja M, Peckham CS, Tookey PA. **Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland.** AIDS 2007;21(8):1019-1026.

**Abstr.** Objective: To explore the association between antiretroviral therapy in pregnancy and premature delivery, birthweight, stillbirth and neonatal mortality, in pregnancies in HIV-infected women delivering between 1990 and 2005. Design: Pregnancies in women with diagnosed HIV infection in the UK and Ireland are notified to the National Study of HIV in Pregnancy and Childhood (NSHPC) through a well-established surveillance scheme. Results: The prematurity rate (< 37 weeks gestation) was higher in women on highly active antiretroviral therapy (HAART) (14.1%, 476/3384) than in women on mono/ dual therapy (10.1%, 107/1061), even after adjusting for ethnicity, maternal age, clinical status and injecting drug use as the source of HIV acquisition [adjusted odds ratio (AOR) = 1.51, 95% confidence interval (CI), 1.19-1.93; P = 0.001]. Delivery at < 35 weeks was even more strongly associated with HAART (AOR=2.34; 95% CI, 1.64-3.37; P < 0.001). The effect was the same whether or not HAART included a protease inhibitor. In comparison with exposure to mono/dual therapy, exposure to HAART was associated with lower birthweight standardized for gestational age (P < 0.001), and an increased risk of stillbirth (AOR = 2.27; 95% CI, 0.96-5.41; P = 0.063). Conclusions: These findings, based on comprehensive population surveillance, demonstrate an increased risk of prematurity associated with HAART, and a possible association with other perinatal outcomes, including stillbirth and birthweight. Although the beneficial effects of antiretroviral therapy on mother-to-child transmission are indisputable, monitoring antiretroviral therapy in pregnancy remains a priority.

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Tuboi SH, Brinkhof MWG, Egger M, Stone RA, Braitstein P, Nash D, Sprinz E, Dabis F, Harrison LH, Schechter M. **Discordant responses to potent antiretroviral treatment in previously naive HIV-1-infected adults initiating treatment in resource-constrained countries - The antiretroviral therapy in low-income countries (ART-LINC) collaboration.** *Journal of Acquired Immune Deficiency Syndromes* 2007;45(1):52-59.

**Abstr.** Objectives: To assess the frequency of and risk factors for discordant responses at 6 months on highly active antiretroviral therapy (HAART) in previously treatment-naive HIV patients from resource-limited countries. Methods: The Antiretroviral Therapy in Low-Income Countries Collaboration is a network of clinics providing care and treatment to HIV-infected patients in Africa, Latin America, and Asia. Patients who initiated therapy between 1996 and 2004, were aged 16 years or older, and had a baseline CD4 cell count were included in this analysis. Responses were defined based on plasma viral load (PVL) and CD4 cell count at 6 months as complete virologic and immunologic (VR+IR+), virologic only (VR+IR-), immunologic only (VR-IR+), and nonresponse (VR-IR-). Multinomial logistic regression was used to assess the association between therapy responses and clinical and demographic variables. Results: Of the 3 111 patients eligible for analysis, 1914 had available information at 6 months of therapy: 1074 (56.1%) were VR+IR+, 364 (19.0%) were VR+IR-, 283 (14.8%) were (VR-IR+), and 193 (10.1%) were VR-IR-. Compared with complete responders, virologic-only responders were older, had a higher baseline CD4 cell count, had a lower baseline PVL, and were more likely to have received a nonstandard HAART regimen; immunologic-only responders were younger, had a lower baseline CD4 cell count, had a higher baseline PVL, and were more likely to have received a protease inhibitor-based regimen. Conclusions: The frequency of and risk factors for discordant responses were comparable to those observed in developed countries. Longer follow-up is needed to assess the long-term impact of discordant responses on mortality in these resource-limited settings.

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Walensky RP, Weinstein MC, Yazdanpanah Y, Losina E, Mercincavage LM, Toure S, Divi N, Anglaret X, Goldie SJ, Freedberg KA. **HIV drug resistance surveillance for prioritizing treatment in resource-limited settings.** *AIDS* 2007;21(8):973-982.

**Abstr.** Background: Sentinel testing programs for HIV drug resistance in resource-limited settings can inform policy on antiretroviral therapy (ART) and drug sequencing. Objective: To examine the value of resistance surveillance in influencing recommendations toward effective and cost-effective sequencing of ART regimens. Methods: A state-transition model of HIV infection was adapted to simulate clinical care in Cote d'Ivoire and evaluate the incremental cost-effectiveness of (1) no ART; (2) ART beginning with a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen followed by a boosted protease inhibitor (PI)-based regimen; and (3) ART beginning with a boosted PI-based regimen followed by an NNRTI-based regimen. Results: At a 5% prevalence of NNRTI resistance, a strategy that started with a PI-based regimen had a smaller health benefit and higher cost-effectiveness ratio than a strategy that started with an NNRTI-based regimen (cost-effectiveness ratio \$910/year of life saved). Results consistently favored initiation with an NNRTI-based regimen, regardless of the population prevalence of NNRTI resistance (up to 76%) and the efficacy of an NNRTI-based regimen in the setting of resistance. The most influential parameters on the cost-effectiveness of sequencing strategies were boosted PI-based regimen costs and the efficacy of this regimen when used as second-line therapy. Conclusions: Drug costs and treatment efficacies, but not NNRTI resistance levels, were most influential in determining optimal HIV drug sequencing in Cote d'Ivoire. Results of surveillance for NNRTI resistance should not be used as a major guide to treatment policy in resource-limited settings.

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