Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Therapy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• In general, HIV-infected women receiving antiretroviral therapy (ART) who present for care during the first trimester should continue treatment during pregnancy, assuming the regimen is tolerated and effective in suppressing viral replication **(AII)**. The Panel recommends that efavirenz be continued in pregnant women receiving efavirenz-based ART who present for antenatal care in the first trimester provided the regimen is resulting in virologic suppression (see text) **(CIII)**.
• Pregnant women receiving and tolerating nevirapine-containing regimens who are virologically suppressed should continue the regimen, regardless of CD4 count **(AIII)**.
• HIV antiretroviral drug-resistance testing is recommended for pregnant women who have detectable viremia (that is, >500–1,000 copies/mL) on therapy (see Failure of Viral Suppression) **(AI)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

In general, women who have been receiving antiretroviral therapy (ART) for their HIV infection should continue that treatment during pregnancy, assuming it is tolerated and effective in suppressing viral replication. Discontinuation of therapy could lead to an increase in viral load with possible decline in immune status and disease progression as well as adverse consequences for the fetus, including increased risk of HIV transmission. Continuation of therapy, therefore, is recommended when pregnancy is identified in HIV-infected women receiving ART.

HIV-infected women receiving ART who present for care during the first trimester should be counseled regarding the benefits and potential risks of administration of antiretroviral (ARV) drugs during this period and that continuation of ART is recommended. There are concerns regarding efavirenz use in the first trimester of pregnancy and potential for neural tube defects, based on preclinical primate data and retrospective case reports (for more details see Special Considerations Regarding the Use of Antiretroviral Drugs by HIV-Infected Pregnant Women and their Infants: Teratogenicity). A recent meta-analysis including data on 1,437 women with first-trimester efavirenz exposure from 19 prospective studies did not find an increased relative risk (RR) of overall birth defects in infants born to women receiving efavirenz-based versus non-efavirenz–based regimens (RR 0.85, 95% confidence interval [CI], 0.6–1.2) and identified 1 neural tube defect, resulting in an incidence of 0.07% (95% CI, 0.002–0.39%).[1] Although a 2- to 3-fold increased incidence of a rare outcome (such as neural tube defects [0.02%–0.2% incidence in the United States]) cannot be ruled out given the limited data on first-trimester efavirenz exposure, the available data suggest that first-trimester exposure is not associated with a large (that is, 10-fold or more) increase in risk of neural tube defects. Analyses from the Italian Group on Surveillance on Antiretroviral Treatment in Pregnancy found that treatment changes during pregnancy significantly increased the risk of incomplete viral suppression at the end of pregnancy.[2] The risk of neural tube defects is restricted to the first 5 to 6 weeks of pregnancy (the neural tube closes at 36–39 days after last menstrual period), pregnancy is rarely recognized before 4 to 6 weeks of pregnancy, and unnecessary changes of ARV drugs in pregnancy may be associated with loss of viral control and, thus, increase risk of transmission to the infant. Therefore, the Panel recommends that efavirenz be continued in pregnant women receiving efavirenz-based ART who present for antenatal care in the first trimester, provided that the regimen is resulting in virologic suppression. In such

situations, additional fetal monitoring (such as with second-trimester ultrasound) should be considered to evaluate fetal anatomy.

Resistance testing should be performed in women who are on therapy but in whom viral replication is not fully suppressed. The results can be used to select a new regimen with a greater likelihood of suppressing viral replication to undetectable levels. Drug resistance testing is generally done in individuals with HIV RNA levels >1,000 copies/mL; however, in persons with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered.

Pregnant women for whom nevirapine-containing regimens are achieving virologic suppression and who are tolerating therapy may be continued on that regimen, regardless of current CD4 T-lymphocyte (CD4-cell) count. Although hepatic toxicity is a concern in women starting a nevirapine-containing regimen who have CD4-cell counts >250 cells/mm^3, an increased risk of hepatic toxicity has not been seen in women receiving nevirapine-based therapy in whom the therapy has produced immune reconstitution.

References

1. Ford N, Calmy A, Mofenson L. Safety of efavirenz in the first trimester of pregnancy: an updated systematic review and meta-analysis. *AIDS*. Nov 28 2011;25(18):2301-2304. Available at http://www.ncbi.nlm.nih.gov/pubmed/21918421.
2. Floridia M, Ravizza M, Pinnetti C, et al. Treatment change in pregnancy is a significant risk factor for detectable HIV-1 RNA in plasma at end of pregnancy. *HIV Clin Trials*. Nov-Dec 2010;11(6):303-311. Available at http://www.ncbi.nlm.nih.gov/pubmed/21239358.