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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Special Situations — Failure of Viral Suppression (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- If an ultrasensitive HIV RNA assay indicates failure of viral suppression (that is, detectable virus) after an adequate period of treatment:
  - Assess resistance and adherence **(AII)**.
  - Consult an HIV treatment expert **(AIII)**.
- Scheduled cesarean delivery is recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of delivery **(AII)**.

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*

A three-pronged approach is indicated for management of women on antiretroviral (ARV) regimens who have suboptimal suppression of HIV RNA (that is, detectable virus at any time during pregnancy using ultrasensitive assays). They should a) be evaluated for resistant virus (if plasma HIV RNA is >500–1,000 copies/mL); b) assessed for adherence, tolerability, incorrect dosing, or potential problems with absorption (such as with nausea/vomiting or lack of attention to food requirements); and, c) consideration should be given to modifying the ARV regimen. Experts in the care of ARV-experienced adults should be consulted, particularly if a change in drug regimen is necessary. Hospitalization may be considered for directly observed drug administration, adherence education, and treatment of comorbidities such as nausea and vomiting.

Among 662 pregnancies followed in Italy between 2001 and 2008, treatment modification during pregnancy was independently associated with an HIV-1 RNA level >400 copies/mL in late pregnancy (adjusted odds ratio, 1.66; 95% confidence interval, 1.07–2.57; $P = 0.024$), highlighting the importance of using potent and well-tolerated regimens during pregnancy to maximize effectiveness and minimize need to modify treatment.[1]

HIV RNA levels should be assessed 2–4 weeks after an ARV drug regimen is initiated or changed to provide an initial assessment of effectiveness.[2] Baseline HIV RNA levels have been shown to affect the time to response in both pregnant and non-pregnant individuals.[3] Most patients with an adequate viral response at 24 weeks have had at least a 1-log copies/mL HIV RNA decrease within 1–4 weeks after starting therapy.[2] Treatment-naive individuals should have HIV RNA <400 copies/mL after 24 weeks of treatment and <50 copies/mL after 48 weeks of treatment. The role of therapeutic drug monitoring in reducing the risk of virologic failure is still undefined.[4]

Because maternal antenatal viral load correlates with risk of perinatal transmission of HIV, suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible. The addition of raltegravir in late pregnancy has been suggested for women who have high viral loads and/or in whom multiple drug-resistant mutations have resulted in incomplete suppression of viremia because of the ability of raltegravir to rapidly suppress viral load (approximately 2-log copies/mL decrease by Week 2 of therapy).[5-8] However, the efficacy and safety of this approach have not been evaluated and only anecdotal reports are available. In the setting of a failing regimen related to nonadherence and/or resistance, there are concerns that the addition of a single agent may further increase risk of resistance and potential loss of future effectiveness with raltegravir. Therefore, at the current time, this approach cannot be recommended. Scheduled cesarean delivery is

recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of delivery (see Transmission and Mode of Delivery).

References

1. 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.
2. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed June 7, 2012.
3. European Collaborative Study, Patel D, Cortina-Borja M, Thorne C, Newell ML. Time to undetectable viral load after highly active antiretroviral therapy initiation among HIV-infected pregnant women. *Clin Infect Dis*. Jun 15 2007;44(12):1647-1656. Available at http://www.ncbi.nlm.nih.gov/pubmed/17516411.
4. Liu X, Ma Q, Zhang F. Therapeutic drug monitoring in highly active antiretroviral therapy. *Expert Opin Drug Saf*. Sep 2010;9(5):743-758. Available at http://www.ncbi.nlm.nih.gov/pubmed/20350281.
5. Grinsztejn B, Nguyen BY, Katlama C, et al. Safety and efficacy of the HIV-1 integrase inhibitor raltegravir (MK-0518) in treatment-experienced patients with multidrug-resistant virus: a phase II randomised controlled trial. *Lancet*. Apr 14 2007;369(9569):1261-1269. Available at http://www.ncbi.nlm.nih.gov/pubmed/17434401.
6. Papendorp SG, van den Berk GE. Preoperative use of raltegravir-containing regimen as induction therapy: very rapid decline of HIV-1 viral load. *AIDS*. Mar 27 2009;23(6):739. Available at http://www.ncbi.nlm.nih.gov/pubmed/19279447.
7. Pinnetti C, Baroncelli S, Villani P, et al. Rapid HIV-RNA decline following addition of raltegravir and tenofovir to ongoing highly active antiretroviral therapy in a woman presenting with high-level HIV viraemia at week 38 of pregnancy. *J Antimicrob Chemother*. Sep 2010;65(9):2050-2052. Available at http://www.ncbi.nlm.nih.gov/pubmed/20630894.
8. McKeown DA, Rosenvinge M, Donaghy S, et al. High neonatal concentrations of raltegravir following transplacental transfer in HIV-1 positive pregnant women. *AIDS*. Sep 24 2010;24(15):2416-2418. Available at http://www.ncbi.nlm.nih.gov/pubmed/20827058.