

## 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

Downloaded from <a href="http://aidsinfo.nih.gov/guidelines">http://aidsinfo.nih.gov/guidelines</a> on 3/18/2013

Visit the AIDS*info* website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <a href="http://aidsinfo.nih.gov/e-news">http://aidsinfo.nih.gov/e-news</a>.

## Lessons from Clinical Trials of Antiretroviral Interventions to Reduce Perinatal Transmission of HIV (Last updated July 31, 2012; last reviewed July 31, 2012)

## **Overview**

One of the major achievements in HIV research was the demonstration by the Pediatric AIDS Clinical Trials Group 076 (PACTG 076) clinical trial that administration of zidovudine to pregnant women and their infants could reduce risk of perinatal transmission by nearly 70%. Following the results of PACTG 076, in the United States and in other resource-abundant countries, implementation of the zidovudine regimen coupled with increased antenatal HIV counseling and testing rapidly resulted in significant declines in transmission. Subsequent clinical trials and observational studies demonstrated that combination antiretroviral (ARV) prophylaxis (initially dual- and then triple-combination therapy) given to a mother antenatally was associated with further declines in transmission to less than 2%. Current estimates indicate that fewer than 200 HIV-infected infants are now born each year in the United States.

Each individual birth of an infected infant is a sentinel event representing missed opportunities and barriers to prevention. <sup>10, 11</sup> Important obstacles to elimination of perinatal transmission in the United States include the continued increase in HIV infection in women of childbearing age; <sup>12</sup> absent or delayed prenatal care, particularly in women using illicit drugs; acute (primary) infection in late pregnancy and in women who are breastfeeding; poor adherence to prescribed ARV regimens in pregnant women; and lack of full implementation of routine, universal prenatal HIV counseling and testing. <sup>9, 11, 13</sup>

Following the results of PACTG 076, researchers began to explore the development of shorter, less expensive prophylactic regimens more applicable to resource-constrained settings. Clinical trials initially focused on shortened zidovudine-alone prophylaxis regimens and moved to evaluating whether combination ARV regimens, such as short-course zidovudine combined with lamivudine, might have improved efficacy over zidovudine alone. Studies also evaluated whether even simpler, less expensive, single-drug regimens, such as single-dose intrapartum/neonatal nevirapine, would be effective and whether combining such regimens with other short-course regimens might result in improved efficacy. These studies have provided important insights into the mechanisms of action of ARV drugs in reducing perinatal transmission and in determining optimal regimens for use in the United States and other resource-rich countries.

## References

- 1. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med*. Nov 3 1994;331(18):1173-1180. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/7935654">http://www.ncbi.nlm.nih.gov/pubmed/7935654</a>.
- 2. Cooper ER, Charurat M, Mofenson L, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr*. Apr 15 2002;29(5):484-494. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/11981365">http://www.ncbi.nlm.nih.gov/pubmed/11981365</a>.
- 3. Wortley PM, Lindegren ML, Fleming PL. Successful implementation of perinatal HIV prevention guidelines. A multistate surveillance evaluation. *MMWR Recomm Rep.* May 11 2001;50(RR-6):17-28. Available at http://www.ncbi.nlm.nih.gov/pubmed/15580801.
- 4. Centers for Disease Control and Prevention. Achievements in public health. Reduction in perinatal transmission of HIV infection--United States, 1985-2005. *MMWR Morb Mortal Wkly Rep*. Jun 2 2006;55(21):592-597. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/16741495">http://www.ncbi.nlm.nih.gov/pubmed/16741495</a>.

- 5. European Collaborative Study. HIV-infected pregnant women and vertical transmission in Europe since 1986. European collaborative study. *AIDS*. 2001;15(6):761-770. Available at <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\_uids=11371691">http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\_uids=11371691</a>.
- Mandelbrot L, Landreau-Mascaro A, Rekacewicz C, et al. Lamivudine-zidovudine combination for prevention of maternal-infant transmission of HIV-1. *JAMA*. Apr 25 2001;285(16):2083-2093. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/11311097">http://www.ncbi.nlm.nih.gov/pubmed/11311097</a>.
- 7. Dorenbaum A, Cunningham CK, Gelber RD, et al. Two-dose intrapartum/newborn nevirapine and standard antiretroviral therapy to reduce perinatal HIV transmission: a randomized trial. *JAMA*. Jul 10 2002;288(2):189-198. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/12095383">http://www.ncbi.nlm.nih.gov/pubmed/12095383</a>.
- McKenna MT, Hu X. Recent trends in the incidence and morbidity that are associated with perinatal human immunodeficiency virus infection in the United States. *Am J Obstet Gynecol*. Sep 2007;197(3 Suppl):S10-16. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/17825639">http://www.ncbi.nlm.nih.gov/pubmed/17825639</a>.
- 9. Rogers MF, Taylor AW, Nesheim SR. Preventing perinatal transmission of HIV: the national perspective. *J Public Health Manag Pract*. Nov-Dec 2010;16(6):505-508. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/20885179">http://www.ncbi.nlm.nih.gov/pubmed/20885179</a>.
- 10. Peters V, Liu KL, Gill B, et al. Missed opportunities for perinatal HIV prevention among HIV-exposed infants born 1996-2000, pediatric spectrum of HIV disease cohort. *Pediatrics*. Sep 2004;114(3):905-906. Available at http://www.ncbi.nlm.nih.gov/pubmed/15342884.
- 11. Whitmore SK, Taylor AW, Espinoza L, Shouse RL, Lampe MA, Nesheim S. Correlates of mother-to-child transmission of HIV in the United States and Puerto Rico. *Pediatrics*. Jan 2012;129(1):e74-81. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/22144694">http://www.ncbi.nlm.nih.gov/pubmed/22144694</a>.
- 12. Whitmore SK, Zhang X, Taylor AW, Blair JM. Estimated number of infants born to HIV-infected women in the United States and five dependent areas, 2006. *J Acquir Immune Defic Syndr*. Jul 1 2011;57(3):218-222. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/21372725">http://www.ncbi.nlm.nih.gov/pubmed/21372725</a>.
- 13. Whitmore SK, Patel-Larson A, Espinoza L, Ruffo NM, Rao S. Missed opportunities to prevent perinatal human immunodeficiency virus transmission in 15 jurisdictions in the United States during 2005-2008. *Women Health*. Jul 2010;50(5):414-425. Available at <a href="http://www.ncbi.nlm.nih.gov/pubmed/20853217">http://www.ncbi.nlm.nih.gov/pubmed/20853217</a>.