Pregnant Women with HIV Who Have Previously Received Antiretroviral Medications but Are Not Currently Receiving Any Antiretroviral Medications

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Panel's Recommendations
• Obtain an accurate history of all prior antiretroviral (ARV) medications used for HIV treatment or prevention of HIV transmission, including virologic efficacy, patient's tolerance of the medications, results of prior resistance testing, and problems with adherence **(AIII)**. • Choose and initiate an antiretroviral therapy (ART) regimen based on results of prior resistance testing, prior ARV drug use, concurrent medical conditions, and current recommendations for ART in pregnancy (see Table 5) **(AII)**. • If HIV RNA is above the threshold for standard genotypic drug resistance testing (i.e., >500 to 1,000 copies/mL), ARV drug-resistance testing should be performed prior to starting an ARV drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) **(AIII)**. • ART should be initiated prior to receiving results of current ARV resistance assays. ART should be modified based on the results of the resistance assay, if necessary **(BIII)**. • If the ART regimen results in insufficient viral suppression, repeat resistance testing and assess other considerations, including adherence, food requirements, and drug interactions **(AII)**. • Consider consulting with an HIV treatment specialist when choosing an ART regimen for women who previously received ARV drugs or modifying ART for those who are not fully suppressed **(BIII).**
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

Pregnant women with HIV who are currently not receiving antiretroviral therapy (ART) may have received antiretroviral (ARV) drugs in the past for their own health and/or prevention of HIV transmission to their infant or their sexual partners (e.g., treatment as prevention).[1] A small number of clinical trials and observational studies have generated information about the effectiveness of ART in individuals who previously received ART to prevent perinatal transmission of HIV.[2–5]

There has been concern that prior, time-limited use of ART during pregnancy to prevent perinatal transmission may lead to resistance and, thus, reduced efficacy if these ARV drugs are used as a part of subsequent ART regimens. Standard genotyping has shown that the rates of resistance after time-limited use of ART appear to be low. Resistance seems to be a concern primarily in patients who received time-limited non-nucleoside reverse transcriptase inhibitor (NNRTI)-based therapy.[6–8] In a comparison between 5,372 ARV-naive pregnant women and 605 women who previously had received ART in the pre-integrase strand transfer inhibitor (INSTI) era (but who were not being treated immediately before the current pregnancy), ARV-experienced women had a small, but statistically significant, increase in the risk of detectable viral load at delivery (adjusted odds ratio 1.27; 95% confidence interval, 1.01–1.60). However, this increased risk only was seen in women who previously received NNRTI-based therapy but not in those who previously received protease inhibitor (PI)-based therapies.[6]

Both standard and sensitive genotyping techniques appear to show a low rate of resistance to PIs after pregnancy-limited use of PI-based ART, but these results reflect assessments in a small number of women.[9,10] Increased risk of treatment failure has not been demonstrated with re-initiation of ART after time-limited use of ART for the prevention of perinatal transmission, especially when using ART regimens with a PI-based regimen or an INSTI.[11] In AIDS Clinical Trials Group (ACTG) 5227, 52 women who previously had received pregnancy-limited ART and who had no evidence of resistance were started on a fixed-dose combination of efavirenz/tenofovir disoproxil fumarate/emtricitabine once daily. After 6 months of therapy, 81% of these women achieved plasma viral loads that were below the limit of detection; the virologic suppression rate was

not affected by the classes of previously used ARV drugs or whether women had received similar ART during one or more previous pregnancies.[2] The data from the French Perinatal Cohort were used to assess the rates of virologic suppression among women who received PI-based ART; ARV-naive women and women who had received ART during previous pregnancies to prevent perinatal transmission had similar rates of viral load suppression at delivery.[11]

ART is now recommended worldwide for everyone with HIV, including all women with HIV during pregnancy and throughout their lives.[12] The data have been reported regarding the benefits of ART for women with higher CD4 T lymphocyte (CD4) cell counts (>350 cells/mm³) and the potential harm of stopping ART after pregnancy in such women. The data from the Promoting Maternal and Infant Safety Everywhere (PROMISE) study (HAART Standard version) showed that women with CD4 counts ≥400 cells/mm³ who were randomized to continue ART postpartum had half the rate of World Health Organization stage 2 and 3 events as those who were randomized to discontinue ART.[13] Furthermore, poor adherence was a common problem for women during the postpartum period in this study. Among women who were randomized to continue ART, 189 of 827 women (23%) had virologic failure. Of the 156 women with virologic failure who had resistance testing, 33% had at least one mutation and 12% had resistance to their current ART regimen. Mutations and resistance occurred more often in women who experienced virologic failure on NNRTI-based regimens. However, most women did not have resistance to their current ART, which suggests nonadherence.[13] When counseling women about the benefits of taking ART during pregnancy and continuing therapy for life, health care providers should emphasize the health benefits of ART and the importance of adherence during the postpartum period (see Postpartum Follow-Up of Women with HIV Infection).

Women may choose to discontinue ART for a variety of reasons, and the length of time off of treatment before pregnancy may vary. A woman's HIV treatment history and all prior drug resistance test results should be considered when choosing ART regimens for pregnant women who previously have received treatment, even when the results of drug resistance testing performed during the current pregnancy are not yet available. Interpretation of resistance testing can be complex because resistance testing is most accurate when performed while an individual is still taking ART or within 4 weeks of discontinuing treatment (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). In the absence of selective drug pressure, resistant virus may revert to wild type; thus, a negative finding does not rule out the presence of archived resistant virus that could re-emerge once ART is restarted (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). Therefore, when selecting a new ART regimen, all information, including regimens received, viral response, laboratory testing (including HLA-B*5701 screening results), any tolerance or adherence problems, food requirements, concomitant medications, prior medical conditions, and results of all prior resistance testing should be considered. In general, ART should be initiated before receiving the results of ARV drug-resistance testing, especially because longer durations of ART during pregnancy have been associated with reduced perinatal transmission rates, compared with shorter treatment periods.[14,15] ART should be modified, when necessary, based on subsequent resistance assay results. Careful monitoring of virologic response is essential (see Monitoring Woman and Fetus During Pregnancy).

A woman may restart a previous ART regimen that successfully suppressed her viral load as long as the regimen was tolerated well and no evidence of resistance to that regimen is indicated. Ideally, the regimen also should be recommended currently as a first-line or alternative regimen for initial ART in pregnancy (see Table 4: What to Start and Table 5). Drugs that are not recommended because of toxicity (stavudine, didanosine, treatment-dose ritonavir) **should not be used**; drugs that are not recommended for initial use because of concerns about viral breakthrough during pregnancy also should be avoided, if possible (see Table 5). Even experienced health care providers may have difficulty with the selection of appropriate ART for women who have advanced HIV disease, a history of extensive prior ART, or previous significant toxicity or nonadherence. In addition to obtaining genotypic resistance testing, it is strongly recommended that specialists in the treatment of HIV be

consulted early in the pregnancy about the choice of a suitable ART regimen for such women.

If ART produces an insufficient viral response (e.g., <1 $\log^{10}$ drop over 2–4 weeks),[16] repeat resistance testing, including testing for resistance to integrase strand transfer inhibitors if indicated (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy), and assess medication adherence, food requirements, and potential drug interactions (including relevant pharmacokinetic studies when available) to inform potential regimen changes. Consultation with an HIV treatment specialist is recommended (see Women Who Have Not Achieved Viral Suppression on ART).

References

1. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365(6):493-505. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21767103.
2. Vogler MA, Smeaton LM, Wright RL, et al. Combination antiretroviral treatment for women previously treated only in pregnancy: week 24 results of AIDS clinical trials group protocol a5227. *J Acquir Immune Defic Syndr*. 2014;65(5):542-550. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24759064.
3. Aziz N, Sokoloff A, Kornak J, et al. Time to viral load suppression in antiretroviral-naive and -experienced HIV-infected pregnant women on highly active antiretroviral therapy: implications for pregnant women presenting late in gestation. *BJOG.* 2013;120(12):1534-1547. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23924192.
4. Huntington S, Thorne C, Anderson J, et al. Response to antiretroviral therapy (ART): comparing women with previous use of zidovudine monotherapy (ZDVm) in pregnancy with ART naive women. *BMC Infect Dis.* 2014;14:127. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24593018.
5. Geretti AM, Fox Z, Johnson JA, et al. Sensitive assessment of the virologic outcomes of stopping and restarting non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy. *PLoS One*. 2013;8(7):e69266. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23874928.
6. French CE, Tookey PA, Cortina-Borja M, de Ruiter A, Townsend CL, Thorne C. Influence of short-course antenatal antiretroviral therapy on viral load and mother-to-child transmission in subsequent pregnancies among HIV-infected women. *Antivir Ther.* 2013;18(2):183-192. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23475123.
7. Perez H, Vignoles M, Laufer N, et al. Low rate of emergence of nevirapine and lamivudine resistance after post-partum interruption of a triple-drug regimen. *Antivir Ther.* 2008;13(1):135-139. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18389908.
8. Lehman DA, Chung MH, Mabuka JM, et al. Lower risk of resistance after short-course HAART compared with zidovudine/single-dose nevirapine used for prevention of HIV-1 mother-to-child transmission. *J Acquir Immune Defic Syndr.* 2009;51(5):522-529. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19502990.
9. Paredes R, Cheng I, Kuritzkes DR, Tuomala RE, Women, Infants Transmission Study Group. Postpartum antiretroviral drug resistance in HIV-1-infected women receiving pregnancy-limited antiretroviral therapy. *AIDS*. 2010;24(1):45-53. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19915448.
10. Gingelmaier A, Eberle J, Kost BP, et al. Protease inhibitor-based antiretroviral prophylaxis during pregnancy and the development of drug resistance. *Clin Infect Dis.* 2010;50(6):890-894. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20166821.

11. Briand N, Mandelbrot L, Blanche S, et al. Previous antiretroviral therapy for prevention of mother-to-child transmission of HIV does not hamper the initial response to PI-based multitherapy during subsequent pregnancy. *J Acquir Immune Defic Syndr.* 2011;57(2):126-135. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21436712.

12. World Health Organization. Update of recommendations on first- and second-line antiretroviral regimens. 2019. Available at: https://www.who.int/hiv/pub/arv/arv-update-2019-policy/en/

13. Currier JS, Britto P, Hoffman RM, et al. Randomized trial of stopping or continuing ART among postpartum women with pre-ART CD4 ≥ 400 cells/mm^3. *PLoS One*. 2017;12(5):e0176009. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28489856.

14. Mandelbrot L, Tubiana R, Le Chenadec J, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clin Infect Dis*. 2015;61(11):1715-1725. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26197844.

15. Townsend CL, Byrne L, Cortina-Borja M, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS*. 2014;28(7):1049-1057. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24566097.

16. Rahangdale L, Cates J, Potter J, et al. Integrase inhibitors in late pregnancy and rapid HIV viral load reduction. *Am J Obstet Gynecol*. 2016;214(3):385 e381-387. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26928154.