Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Pregnant women living with HIV who are currently not receiving antiretroviral therapy (ART) may have received ART in the past for their own health and/or prevention of perinatal transmission in a prior pregnancy. A small number of clinical trials and observational studies have generated information about effectiveness of combination ART in individuals who previously received ART for prevention of perinatal transmission of HIV.1-4

There has been concern that prior, time-limited use of ART during pregnancy for prevention of perinatal transmission may lead to resistance and, thus, reduced efficacy if these antiretroviral (ARV) drugs are used as a part of subsequent ART regimens. Rates of resistance appear to be low, based on standard genotyping, after time-limited use of ART consisting of zidovudine, lamivudine, and nevirapine during pregnancy.5,6 However, minority populations of virus with resistance to nevirapine or lamivudine have been detected using sensitive allele-specific polymerase chain reaction techniques, particularly in women whose virus was inadequately suppressed.6-11 Both standard and sensitive genotyping techniques appear to show a low rate of resistance to protease inhibitors (PIs) after pregnancy-limited use of PI-based ART, but these results reflect assessments in a limited number of women.8,12

Increased risk of treatment failure has not been demonstrated with re-initiation of ART following time-limited use for prevention of perinatal transmission. However, only a limited number of sufficiently large, prospective, observational studies and/or clinical trials have been done to assess the effect of pregnancy-limited ART on the outcome of subsequent treatment. In ACTG 5227, 52 women who had previously 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% achieved plasma viral loads below the limit of detection; the virologic suppression rate was similar regardless of the prior ART drug class or whether women had received similar ART in one or more previous pregnancies.1 Data from the French Perinatal Cohort assessed virologic suppression with PI-based ART administered to women who had received ART during a previous pregnancy for prevention of perinatal

Panel’s Recommendations

- Obtain an accurate history of all prior antiretroviral (ARV) regimens used for treatment of HIV disease or prevention of transmission, including virologic efficacy, tolerance of the medications, results of prior resistance testing, and problems with adherence (AIII).
- Choose and initiate a combination antiretroviral therapy (ART) regimen based on results of prior resistance testing, prior ARV use, concurrent medical conditions, and current recommendations for ART in pregnancy, avoiding drugs with potential known adverse effects for the mother or fetus/infant (AII).
- If HIV RNA is above the threshold for resistance testing (i.e., >500–1,000 copies/mL), ARV resistance studies should be performed prior to starting an ARV drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AI).
- In general, ART should be initiated prior to receiving results of current ARV resistance studies because longer ART has been associated with reduced transmission rates compared to shorter treatment periods (BIII). ART should be modified based on the results of the resistance assay, if necessary (AIII).
- If the ART regimen results in insufficient viral suppression, repeat resistance testing and assess other considerations including adherence and drug interactions (BII).
- Consider consulting with an HIV treatment specialist about the choice of ART regimen to initiate in women who previously received ARV drugs or to modify ART in 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
transmission. No differences in rates of undetectable viral load at delivery were noted among ARV-naive women when compared with those who received ART during previous pregnancies or according to type of ART previously received.\textsuperscript{13} In addition, the National Study of HIV in Pregnancy and Childhood in the United Kingdom and Ireland found no increased risk of perinatal transmission in sequential pregnancies compared with a single pregnancy when most women received ART for prevention of perinatal HIV transmission.\textsuperscript{14} However, in a comparison between 5,372 ARV-naive pregnant women and 605 women who had previously received ART (but were not being treated immediately prior to the current pregnancy), ARV-experienced women had a small but significant increase in the risk of detectable viral load at delivery (aOR 1.27; 95% CI, 1.01–1.60). This risk was confined to those ARV-experienced women who received non-nucleoside reverse transcriptase inhibitor-based as opposed to PI-based therapy.\textsuperscript{15}

Women may choose to discontinue ART for a variety of reasons, and the length of time off treatment prior to pregnancy may vary. Choice of ART in pregnant women who have been previously treated should be made based on treatment history and all prior drug resistance testing results, even if results of drug resistance testing obtained during the current pregnancy are not yet available. Interpretation of resistance testing can be complex because it is most accurate if performed while an individual is still taking ART or within 4 weeks of treatment discontinuation. In the absence of selective drug pressure, resistant virus may revert to wild-type virus and, although detection of drug-resistance mutations is informative for choosing a regimen, a negative finding does not rule out the presence of archived drug-resistant virus that could re-emerge once ART is restarted. Therefore, when selecting a new ART regimen, all information including regimens received, viral response, laboratory testing (including HLA-B*5701 results), any tolerance or adherence problems, concomitant medications, prior medical conditions, and the results of resistance testing should be taken into consideration. In general, ART should be initiated prior to receiving results of ARV drug-resistance studies, especially because longer duration of ART has been associated with reduced transmission rates compared to shorter treatment periods.\textsuperscript{16,17} ART should be modified, if necessary, based on subsequent resistance assay results. Careful monitoring of virologic response is essential.

It is reasonable to restart the same ART regimen in a woman with a history of prior ART associated with successful suppression of viral load assuming that it was well tolerated, has no evidence of resistance to that ART, and (preferably) is currently recommended as first-line or an alternate ART regimen for initial ART in pregnancy (see Table 6: What to Start). Drugs not recommended for initial use because of toxicity (stavudine, didanosine, treatment-dose ritonavir) should not be used; drugs not recommended for initial use because of concerns about viral breakthrough during pregnancy should also generally be avoided. Even experienced healthcare providers may have difficulty with the selection of appropriate ART for women with advanced HIV disease, a history of extensive prior ART, or previous significant toxicity or nonadherence to ARV drugs. 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 drop over 4–8 weeks), repeat resistance testing and assess medication adherence and potential drug interactions (including, if available, relevant pharmacokinetic studies) to inform potential regimen changes. Consultation with an HIV treatment specialist is recommended.

References


