Pregnant Women Living with HIV Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications (Last updated December 7, 2018; last reviewed December 7, 2018)

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, the patient’s 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 (see Table 7) (AII).
- If HIV RNA is above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL), ARV resistance testing should be performed prior to starting an ARV drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AIII).
- In general, ART should be initiated prior to receiving results of current ARV resistance studies, because longer use of ART during pregnancy has been associated with reduced transmission rates to the infant compared to shorter treatment periods. 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 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

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% 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.1 Data from the French Perinatal Cohort

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was used to assess virologic suppression with PI-based ART administered to women who had received ART during a previous pregnancy for prevention of perinatal transmission. ARV-naive women and women who received ART during previous pregnancies had similar rates of undetectable viral load at delivery. The type of ART previously received did not affect the rate of undetectable viral load at delivery. 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. However, in a comparison between 5,372 ARV-naive pregnant women and 605 women who had previously received ART (but who 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 (adjusted odds ratio [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 (NNRTI)-based therapy, as opposed to those who received PI-based therapy.

ART is now recommended worldwide for women living with HIV during pregnancy and throughout their lives. 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 ARV after pregnancy in such women. Data from the HAART Standard version of the PROMISE study showed that women with CD4 cell counts ≥400 cells/mm³ who were randomized to continue ART postpartum had half the rate of WHO Stage 2 and 3 events as those who discontinued ART. Further, poor adherence was a common problem for women during the postpartum period in this study. Among women randomized to continue ART, 189 of 827 women (23%) had virologic failure. Of the 156 women with virologic failure who had resistance testing, 12% had resistance to their current ART (which was more common in women experiencing failure on NNRTI-based regimens), but 66% did not have resistance to their current regimen, suggesting nonadherence. When counselling women about the benefits of taking ART during pregnancy and continuing for life, health care providers should emphasize the health benefits of maintaining ART and the importance of adherence during the postpartum period (see Postpartum Follow-Up of Women Living with HIV Infection).

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 test results, 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 it is most accurate when 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 and, although detection of drug resistance mutations is informative for choosing a regimen, a negative finding does not rule out the presence of archived 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, food requirements, 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 the results of ARV drug-resistance studies, especially because longer duration of ART has been associated with reduced transmission rates compared to shorter treatment periods. ART should be modified, when necessary, based on subsequent resistance assay results. Careful monitoring of virologic response is essential.

A woman may restart a previous ARV regimen that successfully suppressed her viral load, if the regimen was well tolerated, there is no evidence of resistance to that regimen, and (preferably) the regimen is currently recommended as first-line or an alternative regimen for initial ART in pregnancy (see Table 6: What to Start). Drugs that are not recommended for initial use 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 should also be avoided. 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 drop over 2–4 weeks), repeat resistance testing and assess medication adherence, food requirements, and potential drug interactions (including, if available, relevant pharmacokinetic studies) to inform potential regimen changes. Consultation with an HIV treatment specialist is recommended (see Lack of Viral Suppression).

References


