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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HIV-2 infection is endemic in West African countries, including Ivory Coast, Ghana, Cape Verde, The Gambia, Mali, Senegal, Liberia, Guinea, Burkina Faso, Nigeria, Mauritania, Sierra Leone, Guinea Bissau, Niger, Sao Tome, and Togo. It is also endemic in Angola, Mozambique, and in parts of India. It also occurs in countries such as France and Portugal, which have large numbers of immigrants from these regions.

HIV-2 remains rare in the United States. Between 1998 and 2010, 242 HIV-2 cases were reported to the Centers for Disease Control and Prevention (CDC), with 166 cases meeting the criteria for HIV-2 diagnosis. These 166 cases constituted only 0.01% of the >1.4 million U.S. cases of HIV infection.

Of the 50 women aged 15 to 44 years at diagnosis, 24 (48%) were pregnant at HIV-2 diagnosis or became pregnant after diagnosis. HIV-2 infection should be suspected in pregnant women who are from—or who have partners from—countries in which the disease is endemic and who have positive results on an HIV-1/HIV-2 antibody or HIV-1/HIV-2 antigen/antibody immunoassay. They should be tested with a supplemental HIV-1/HIV-2 antibody differentiation assay. If they have only HIV-2 infection, the test will be negative for HIV-1 antibodies and positive for HIV-2 antibodies (AII).

Pregnant women living with HIV-1/HIV-2 coinfection should be treated as per guidelines for HIV-1 monoinfection, but using antiretroviral drugs that are active against HIV-2 (see below).

No randomized clinical trials have been performed to address when to start treatment or what the optimal treatment is for HIV-2 infection (AIII). A regimen with two nucleoside reverse transcriptase inhibitors and certain boosted protease inhibitors or integrase strand transfer inhibitors is recommended for all pregnant women living with HIV-2 infection (AIII).

Non-nucleoside reverse transcriptase inhibitors and enfuvirtide are not active against HIV-2 and should not be used (AIII).

All infants born to mothers living with HIV-2 infection should receive the 4-week zidovudine prophylactic regimen (BIII).

In the United States, where safe infant formula is readily available, breastfeeding is not recommended for infants of mothers living with HIV-2 infection (AIII).

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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
HIV-2 has a longer asymptomatic phase than HIV-1, with a slower progression to AIDS. The most common mode of HIV-2 transmission is through heterosexual sex. HIV-2 is less infectious than HIV-1, with a 5-fold lower rate of sexual transmission and 20- to 30-fold lower rate of vertical transmission.\(^{3,12,13}\) Several studies confirm that rates of perinatal transmission of HIV-2 are low with and without interventions (0% to 4%), which may be a result of reduced plasma viral loads and less cervical viral shedding in women with HIV-2 than in women with HIV-1 infection.\(^{14-17}\) HIV-2 also can be transmitted through breastfeeding. HIV-2 infection does not protect against HIV-1, and dual infection, which carries the same prognosis as HIV-1 monoinfection, can occur.\(^{18}\)

Pregnant women living with HIV-1/HIV-2 coinfection should be treated according to the guidelines for patients with HIV-1 monoinfection, making sure that the antiretroviral therapy (ART) regimen chosen is also appropriate for treatment of HIV-2 (see below). Once treatment is started, ART should be continued postpartum, as is recommended for all patients living with HIV-1 infection. A systematic review analyzed data collected from 1996 to 2012 on treatment outcomes among nonpregnant patients living with HIV-2 infection. The review reported a heterogeneity of treatment outcomes among patients who initiated ART, especially in resource-limited settings.\(^{19}\) Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and enfuvirtide are not active against HIV-2 and should not be used for treatment or prophylaxis.\(^{20,21}\) HIV-2 has variable susceptibility to protease inhibitors (PIs), with lopinavir, saquinavir, and darunavir having the most activity.\(^{22}\) The integrase strand transfer inhibitors (INSTIs) raltegravir, elvitegravir, and dolutegravir also appear to be effective against HIV-2.\(^{23-30}\) Although dolutegravir may be able to rescue a failing raltegravir-based regimen in a person with HIV-2, a study has reported the emergence of dolutegravir resistance mutations in people living with HIV-2.\(^{31}\)

The care of pregnant women living with HIV-2 monoinfection has been based on expert opinion. A regimen with two NRTIs and a ritonavir-boosted PI or an INSTI currently is recommended for all pregnant women living with HIV-2 infection. Based on efficacy and available data on safety in pregnant women with HIV-1 infection, darunavir/ritonavir, lopinavir/ritonavir, raltegravir or dolutegravir (after the first trimester) plus abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine or lamivudine is preferred. Dolutegravir should not be initiated during the first trimester due to concerns about a possible increased risk of neural tube defects in infants. See Table 6, Table 7, and Interim Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy in Recommendations for Use of Antiretroviral Drugs During Pregnancy. Zidovudine/lamivudine can be used as an alternative dual-NRTI backbone.\(^{37,38}\) NNRTIs should not be used, because they are not active against HIV-2.

There are no data to address whether treatment should be continued after pregnancy in women living with HIV-2 monoinfection. To date, no randomized trials have addressed the question of an optimal treatment strategy for HIV-2 infection, although clinical trials are underway. The Adult and Adolescent Guidelines note that although the optimal CD4 T lymphocyte (CD4) cell count threshold to initiate ART in HIV-2 monoinfection is unknown, therapy should be started before there is clinical progression.\(^{39}\) For pregnant women living with HIV-2 infection who have CD4 cell counts >500 cells/mm\(^3\) and no significant clinical disease (and who currently do not require treatment for their own health), some experts would stop ART postpartum; however, many experts would recommend continuing treatment after pregnancy in women living with HIV-2 monoinfection, as is recommended for HIV-1 monoinfection or HIV-1/HIV-2 coinfection.

All infants born to mothers living with HIV-2 should receive a 4-week zidovudine prophylaxis regimen.\(^{38}\) The possible risks and benefits of ARV prophylaxis should be discussed with the mothers. The rationale for
zidovudine prophylaxis in this clinical situation is based on the inability to monitor HIV-2 plasma viral load in the mother and the lack of nevirapine activity against HIV-2, which precludes its use as prophylaxis.

There is no evidence that scheduled cesarean delivery in women prevents HIV-2 vertical transmission. The risk to infants from breastfeeding is lower for HIV-2 than for HIV-1, but breastfeeding should be avoided in the United States and other countries where safe infant formula is readily available.\textsuperscript{15}

Infants born to mothers living with HIV-2 infection should be tested for HIV-2 infection with HIV-2-specific virologic assays at time points similar to those used for HIV-1 testing.\textsuperscript{40} Quantitative HIV-2 plasma RNA viral load testing for clinical care is available from the University of Washington\textsuperscript{8} and the New York State Department of Health.\textsuperscript{9} Antibody testing of infants (e.g., with the Bio-Rad Laboratories Multispot HIV-1/HIV-2 test) can also be performed at age 18 months to confirm clearance of HIV-2 antibodies.\textsuperscript{38}

References


