What's New in the Pediatric Guidelines

Updated: January 31, 2024
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The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) has reviewed and updated one section of the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* that is developed in collaboration with the Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. The changes are highlighted in yellow in the PDF version of the guidelines.

Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure

- This section has been retitled to align with updates in other sections, with revisions and updates made to bulleted recommendations and throughout the text to provide added detail, new data, and clarification.
- The Panel recommends that when acute HIV infection is suspected during pregnancy, the intrapartum period, or while breastfeeding, a plasma HIV RNA assay should be performed in conjunction with an antigen/antibody immunoassay.

April 11, 2023

When to Start

- The section summary has been revised to clarify that rapid initiation of antiretroviral therapy (ART), defined as therapy initiated immediately or within days of HIV diagnosis, is recommended except for children with cryptococcal meningitis, disseminated *Mycobacterium avium* Complex Disease, or *Mycobacterium tuberculosis*. Because of concerns regarding the risk of immune reconstitution inflammatory syndrome, ART initiation may be deferred until the optimal timing relative to treatment of the opportunistic infection. Timing of ART initiation in these cases should be discussed with a pediatric HIV specialist. See the Guidelines for the Prevention and Treatment of Opportunistic Infections in Children With and Exposed to HIV and the World Health Organization Updated Recommendations on HIV Prevention, Infant Diagnosis, Antiretroviral Initiation, and Monitoring, March 2021.

Clinical and Laboratory Monitoring of Pediatric HIV Infection

- The section now describes several methods to obtain regular weight and height measurements in addition to HIV clinic visits. Cooperative children can be weighed and height measured at home if a scale and measuring tape are available, with simple instructions for continuity, or directly observed during a synchronous visit or obtained from recent pediatric or other specialty in-office visit.

- Table 5. CD4 Cell Counts and Percentages in Healthy Children: Distribution by Age has been added to the section.
- Table 6. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy has been updated.
- Initial laboratory screening for infants and children now includes HLA-B*5701 testing to allow for possible abacavir initiation. An alternative ARV drug should be used if the HLA-B*5701 test result is positive.
- The Panel has added guidance about viral load monitoring for adolescents initiating long-acting cabotegravir and rilpivirine (LA-CAB and RPV).
- To address issues related to biologic variability in HIV RNA (viral load), the Panel has added clarification of clinically significant plasma viral load changes in infants aged <2 years (>0.7 $\log_{10}$ copies/mL, a fivefold difference) and in children aged ≥2 years (>0.5 $\log_{10}$ copies/mL, a threefold difference).

What Not to Start: Regimens Not Recommended for Use Antiretroviral-Naive Children

- Content regarding some drugs that are not recommended for initial therapy has been reorganized.

Special Considerations for Antiretroviral Therapy Use in Adolescents With HIV

- The Panel noted that LA-CAB and RPV could be considered to improve or support ART adherence in adolescents aged ≥12 years and weighing ≥35 kg who are virally suppressed and also noted that data about the use of LA-CAB and RPV in those with adherence concerns are still emerging.
- Based on recent data about a higher prevalence of attempted suicide in adolescents with HIV compared to HIV-exposed but uninfected adolescents, providers who are caring for adolescents with HIV should incorporate screening for suicidality into other mental health and psychiatric screenings, referring patients to age-appropriate services as needed.

Adherence to Antiretroviral Therapy in Children and Adolescents With HIV

- The Panel points out that the growing use of telemedicine visits, which allow remote and often face-to-face contact, provides new opportunities to support families and visualize ART handling and swallowing, as well as to conduct directly observed therapy in the home setting.
- Table 16. Strategies to Improve Adherence to Antiretroviral Medications has been updated to address monitoring adherence, specific barriers to adherence, and strategies that may help to improve adherence, such as participation in camp programs and referrals to counseling and mental health programs.

Management of Medication Toxicity or Intolerance

- Tables for Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations have been reviewed with updates regarding associated ARVs, onset and

clinical manifestations, estimated frequency, risk factors, prevention and monitoring, and management where indicated.

  - Table 17a. Central Nervous System Toxicity. The table now includes neuropsychiatric symptoms and other central nervous system manifestations associated with cabotegravir.

Management of Children Receiving Antiretroviral Therapy

- Modifying Antiretroviral Regimens in Children With Sustained Virologic Suppression on Antiretroviral Therapy and Table 18. Examples of Changes in Antiretroviral Regimen Components for Children With Sustained Virologic Suppression have been updated to incorporate the most recent switch options in line with pediatric ARV drug approvals and Panel recommendations.
- While oral two-drug regimens are not approved for use in children or for initial therapy, the Panel notes that they may be considered for when simplification of ART or avoidance of nucleoside reverse transcriptase inhibitors is needed. Because adolescents may have difficulties adhering to therapy, close monitoring with viral load testing is recommended.
- Recognizing and Managing Antiretroviral Treatment Failure and Table 20. Options for Regimens With at Least Two Fully Active Agents to Achieve Virologic Suppression in Patients With Virologic Failure and Evidence of Viral Resistance have been updated to incorporate new data and ARV options in the context of treatment failure.

Appendix A: Pediatric Antiretroviral Drug Information

Drug sections and fixed-dose combination (FDC) Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-packaged Formulation, by Drug Class and Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents in this appendix were reviewed and updated to include recent pediatric data, dosing and safety information, and U.S. Food and Drug Administration approvals of new formulations and FDCs. Significant changes are summarized below:

- The Bictegravir section was updated to include additional information related to splitting, dissolving, or crushing bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) tablets; crushing tablets is not recommended.
- The Panel notes that the current raltegravir dosing regimen with two dose changes in the first month of life may be challenging for some families; the Raltegravir section now includes guidance from some experts on simplifying medication teaching and minimizing dosing changes.

January 31, 2023

Infant Feeding for Individuals with HIV in the United States

Updated recommendations for infant feeding are now included as a shared section in the Perinatal Guidelines.

The Panel recommends that people with HIV receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding. Counseling about infant feeding should begin prior to conception or as early as possible in pregnancy; information about and plans for infant

feeding should be reviewed throughout pregnancy and again after delivery **(AIII).** During counseling, people should be informed that—

- Replacement feeding with properly prepared formula or pasteurized donor human milk from a milk bank eliminates the risk of postnatal HIV transmission to the infant **(AI).**
- Achieving and maintaining viral suppression through antiretroviral (ARV) therapy during pregnancy and postpartum decreases breastfeeding transmission risk to less than 1%, but not zero **(AI).**

Replacement feeding with formula or banked pasteurized donor human milk is recommended to eliminate the risk of HIV transmission through breastfeeding when people with HIV are not on antiretroviral therapy (ART) and/or do not have a suppressed viral load during pregnancy (at a minimum throughout the third trimester) and at delivery **(AI).**

Individuals with HIV who are on ART with a sustained undetectable viral load and who choose to breastfeed should be supported in this decision **(AIII).**

Individuals with HIV who choose to formula feed should be supported in this decision; potential barriers to formula feeding should be identified and addressed **(AIII).**

Content about counseling and management of individuals who choose to breastfeed was updated, with added content on situations in which to consider stopping or modifying breastfeeding.

Diagnosis of HIV Infection in Infants and Children

This section now provides additional guidance about HIV diagnostic testing for infants with perinatal HIV exposure who are being breastfed, with time points for testing listed in Table 3. Recommended Virologic Testing Schedules for Infants Who Were Exposed to HIV According to Risk of Perinatal HIV Acquisition at and After Birth.

A subsection was added with information about HIV testing for infants who were being breastfed at the time of maternal HIV diagnosis.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

When the criteria for low risk of perinatal HIV transmission are met, the Panel now recommends that infants receive 2 weeks of zidovudine (ZDV) prophylaxis **(BII),** rather than 4 weeks (see Table 12. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn).

- The criterion for viral suppression was further defined as at least two consecutive tests with HIV RNA levels <50 copies/mL obtained at least 4 weeks apart.

Infants born to individuals who do not meet criteria for low risk for perinatal HIV transmission but who have a viral load <50 copies/mL at or after 36 weeks should receive ZDV for 4 to 6 weeks **(BII).**

The Panel clarified the duration of ARVs for newborns at high risk of perinatal acquisition. Presumptive HIV therapy with three-drug regimens should be administered from birth for 2 to 6 weeks (see Tables 12 and 13); if the duration of the three-drug regimen is shorter than 6 weeks, ZDV should be continued alone to complete a total of 6 weeks of prophylaxis.

All premature infants <37 weeks gestation who are not at high risk of perinatal acquisition of HIV should receive ZDV for 4 to 6 weeks **(BII).**

New subsections and Table 14. Infant Antiretroviral Prophylaxis for Newborns of Mothers with Sustained Viral Suppression Who Breastfeed were added to address ARV prophylaxis for newborns at low risk of perinatal HIV transmission who are breastfed and to provide information about breastfeeding in newborns at high risk of perinatal HIV acquisition.