NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

MASAC Document #154

MASAC RECOMMENDATIONS REGARDING THE USE OF ANTIRETROVIRAL THERAPY IN THE TREATMENT OF HIV INFECTION (Revised November 2003)

The following document was approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation on November 8, 2003, and adopted by the NHF Board of Directors on November 9, 2003.

Much has changed since the previous MASAC Recommendation #124. Although the changes are summarized briefly below, MASAC strongly recommends that providers refer to the source document referenced below, entitled "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents," for specific information, available at http://aidsinfo.nih.gov/guidelines/.

Because of the complexity of these issues, consultation with an HIV/infectious disease specialist is strongly recommended.

HIV RNA (Viral Load) and CD4+ T Cell Count Testing

HIV RNA Viral load (VL) testing is essential in decisions to initiate or change antiretroviral therapy (ART). It is recommended that VL be performed at diagnosis, before and 2-8 weeks after initiation or change in antiretroviral treatment, and then every 3-6 months. A significant change in VL is considered to be at least a 3-fold decrease or a 3-fold increase in VL. The goal of antiretroviral therapy is to eradicate VL to <50 copies/ml; the absence of virologic response should prompt reassessment of the patient and consideration for change in drug regimen.

Testing for Antiretroviral Drug Resistance

Testing for antiretroviral drug resistance is an adjunct to guide treatment. Drug resistance may be performed by either genotyping or phenotype resistance assays. In general, the presence of drug resistance is associated with failure of antiretroviral treatment and failure to suppress HIV viral load. Genotyping detects mutations in viral genes, while phenotyping measures the ability of the virus to grow in the presence of certain antiretroviral drugs. In general, resistance testing is used when there has been suboptimal viral load suppression after initiation of treatment.

Initiation of Antiretroviral Therapy (ART)

Initiation of ART is recommended in individuals with CD4 <200/microliter, in those with CD4 200- 350/microliter and HIV VL > 20,000 copies/ml, and in those with CD4 >350/microliter and HIV VL >60,000 copies/ml.

Adherence to Antiretroviral Therapy

Decisions regarding treatment depend also on whether the patient is ready to adhere to an antiretroviral regimen. Good adherence is associated with sustained virologic control, while poor adherence is associated with virologic failure and increased morbidity and mortality. The many factors that may influence adherence, including gender, race, socio-economic status, educational level, and prior drug use, should be considered in decisions regarding treatment. Good patient-physician communication and a trusting relationship are essential to the success of treatment.

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Antiretroviral Therapy in Advanced Disease

All patients with advanced disease meeting the 1993 CDC definition of AIDS (CD4 < 200, presence of opportunistic infection, AIDS-related malignancy, recurrent bacterial infections) should be treated with ART. Other clinical issues to be considered include drug toxicity, adherence to treatment, drug interactions, and laboratory abnormalities associated with treatment. A maximally suppressive regimen should be used.

Antiretroviral Therapy-related Adverse Events

ART may be associated with adverse clinical events, including lactic acidosis, hepatic steatosis, hyperglycemia, diabetes mellitus, fat maldistribution, excessive bleeding in individuals with hemophilia, osteopenia, osteoporosis, and rash. Ongoing monitoring for drug toxicity is strongly advised, and treatment should be discontinued if medically indicated because of unacceptable toxicity.

Interruption of Therapy

ART may be stopped for serious adverse events. However, there are insufficient data in the above situations to make firm recommendations. Further research is needed in each of these areas.

Changing Antiretroviral Therapy and Available Therapeutic Options

It should be determined why a drug regimen has failed (i.e., viral resistance, drug toxicity, or poor adherence). In general, drug toxicity may require replacement of one drug in a regimen, while viral resistance may require resistance testing and consideration of changing at least two drugs in a regimen. Poor adherence should prompt a discussion of the underlying reasons and the expectations for future compliance and may include a mental health or social work assessment. Criteria for changing therapy include: 1) less than 0.5-0.75 $\log_{10}$ reduction in HIV RNA by 4 weeks after drug initiation, or less than 1 $\log_{10}$ reduction by 8 weeks; 2) repeated detection of HIV RNA after initial suppression; 3) confirmed > 3-fold increase in viral load; 4) undetectable viral load with double nucleoside therapy; 5) persistently declining CD4+ T cell counts; or 6) clinical deterioration.

Treatment of Acute HIV Infection

There are ongoing clinical trials to evaluate the benefit of long-term potent ART after acute infection. Information at this time is limited, but preliminary data suggest that combination therapy may be beneficial both clinically and on markers of disease. Potential benefits include 1) suppressing viral replication and decreasing the magnitude of viral dissemination throughout the body; 2) decreasing the severity of acute disease; 3) lowering the viral set point after initial infection; 4) reducing the rate of viral mutation; 5) reducing the risk of viral transmission; and 6) preserving immune function.

Antiretroviral Therapy in Adolescents

Adolescents may have been infected perinatally (infected mother), in young childhood (e.g., hemophilia, transfusion), or in adolescence (e.g., IV drug, sexual). ART drugs and dosing should be based on Tanner puberty stage and not on specific age. Adolescents in the midst of a growth spurt should be monitored carefully for drug efficacy and toxicity.

Antiretroviral Therapy in the Pregnant Woman

ART in pregnancy should not be withheld unless the adverse effect risks outweigh the potential benefits. Combination therapy is the recommended standard for HIV-infected non-pregnant adults. For pregnant women, a three-part regimen of zidovudine, beginning at 14 weeks gestation

and continued throughout pregnancy, then given intravenously during labor and to the newborn for the first six weeks of life, is recommended. Pregnancy should not preclude the use of optimal therapeutic regimens. Additional considerations include 1) potential dose changes due to physiologic changes in pregnancy; 2) potential effects of ART on the pregnant woman; 3) risks of perinatal HIV transmission; and 4) potential effects of ART on the fetus and newborn. Consideration should be made in those women not already on ART to delay ART until after 10 to 12 weeks of gestation during organogenesis and potential teratogenic effects. If clinical, virologic, or immunologic parameters are such that therapy would be otherwise recommended for nonpregnant individuals, it is generally recommended that treatment be initiated, regardless of gestational age, with standard combination ART. Women already receiving ART should consider continuing it during pregnancy, as there are few data to support or refute teratogenic risk. Based on animal studies, efavirenz and hydroxyurea should be avoided during the first trimester. Because early pregnancy may mimic symptoms of toxicity (e.g., lactic acidosis), careful monitoring is essential (see MASAC Recommendation #122).

References:

1. Panel on Clinical Practices for Treatment of HIV Infection. U. S. Department of Health and Human Services guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. November 10, 2003. Available at http://aidsinfo.nih.gov/guidelines/.
2. Centers for Disease Control. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* 1992;41:(No. RR-17);1-19.

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