ART for HIV: Recommendations from the International Antiviral Society—USA Panel

Key Points for Practice

- To prevent transmission, persons with HIV infection should be treated with ART, despite CD4 cell count.
- The following should be considered when changing a person's ART regimen: previous exposure to therapy, resistance history, medication interactions, and medication tolerability.
- After starting or modifying a patient's ART, measurement of HIV-1 RNA should be performed after four weeks.
- Although routine therapeutic drug monitoring is typically not necessary, monitoring for toxicity using laboratory testing is recommended.

From the *AFP* Editors

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Evidence has shown that antiretroviral therapy (ART) for treatment of human immunodeficiency virus (HIV) infection is effective in preventing transmission among couples. Additionally, newer ART medications have greater effectiveness and tolerability and lower toxicity, making treatment for longer timeframes more easily achievable. ART can even be effective in persons with HIV infection for whom treatment previously failed or in those with resistance to medications. The International Antiviral Society—USA Panel has provided recommendations for management of HIV infection with ART.

Recommendations

INITIATION

To prevent transmission, persons with HIV infection should be treated with ART, despite CD4 cell count; however, the strength of this recommendation is greater the lower a patient's CD4 cell count (e.g., 500 per μL or less). Regardless of whether patients with acute HIV infection have symptoms, they should be offered ART.

For persons with HIV infection with CD4 cell counts greater than 500 per μL, the strength of recommendation for treatment with ART increases in those with certain conditions, including nephropathy and chronic hepatitis B virus infection, and in women who are pregnant. In persons with opportunistic infections or diseases, and in those with AIDS-defining illnesses, ART should be started as soon as feasible after diagnosis (within two weeks if possible). In persons with cryptococcal meningitis, ART should be considered early when there is access to experts in treating both the cryptococcal and HIV infections. In persons infected with HIV and tuberculosis, ART should be initiated within two weeks of tuberculosis treatment when the CD4 count is less than 50 per μL. In those with tuberculosis and a CD4 cell count of 50 per μL or greater, ART should initiated within eight to 12 weeks. If a patient has tuberculous meningitis, ART should be initiated within two to eight weeks, and experts should be consulted to assist with treatment.

MODIFICATION: PATIENTS WHO ARE TREATMENT EXPERIENCED

When opting to change a person's ART regimen, previous exposure to therapy, resistance history, and medication interactions should be taken into account, as should a history of toxic effects or not being able to tolerate therapy. If a patient has a known resistance to multiple medications, physicians should consider using a boosted protease inhibitor and medications from newer classes (e.g., integrase strand transfer inhibitor, maraviroc [Selzentry]); however, the patient's resistance history, viral tropism, and all available therapy options should be taken into account when doing so. Patients should not be prescribed a regimen consisting solely of a boosted protease inhibitor, unless there are no other alternatives. When modifying a patient's therapy plan, maintaining virologic suppression is essential, and changing or simplifying ART in persons with virologic suppression is typically safe as long as previous treatments and a patient's resistance history are taken into account. Additionally, when changing a patient's ART from a ritonavir (Norvir)-boosted protease inhibitor to a medication with low resistance thresholds (e.g., nonnucleoside reverse transcriptase inhibitors, protease inhibitors that are unboosted), the activity of the nucleoside reverse transcriptase inhibitors must be ensured. ▶

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In the per-protocal analysis set, females accounted for 57.2% of participants in the Fluzone High-Dose group and 56.1% of participants in the Fluzone group. In both groups, the median age was 72.2 years (range 65 through 100 years). Overall, most participants in the study were Caucasian (95%); approximately 4% of study participants were Black, and approximately 6% reported Hispanic ethnicity.

The primary endpoint of the study was the occurrence of laboratory-confirmed influenza (as determined by culture or polymerase chain reaction) caused by any influenza viral type/subtype in association with influenza-like illness (ILI), defined as a new onset (or exacerbation) of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature >99.0°F, chills, tiredness, headaches or myalgia. Participants were monitored for the occurrence of a respiratory illness by both active and passive surveillance, starting 2 weeks post-vaccination for approximately 7 months. After an episode of respiratory illness, nasopharyngeal swab samples were collected for analysis; attack rates and vaccine efficacy were calculated (see Table 3).

Table 3: Study 2[a]: Relative Efficacy Against Laboratory-Confirmed Influenza[b] Regardless of Similarity to the Vaccine Components, Associated with Influenza-Like Illness[c], Adults 65 Years of Age and Older

	Fluzone High-Dose N[d]=15,892 n[e] (%)	Fluzone N[d]=15,911 n[e] (%)	Relative Efficacy % (95% CI)
Any type/subtype[f]	227 (1.43)	300 (1.89)	24.2 (9.7; 36.5)[g]
Influenza A	190 (1.20)	249 (1.56)	23.6 (7.4; 37.1)
A (H1N1)	8 (0.05)	9 (0.06)	11.0 (-159.9; 70.1)
A (H3N2)	171 (1.08)	222 (1.40)	22.9 (5.4; 37.2)
Influenza B[h]	37 (0.23)	51 (0.32)	27.4 (-13.1; 53.8)

[a] NCT01427309
[b] Laboratory-confirmed: culture- or polymerase-chain-reaction-confirmed
[c] Occurrence of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature >99.0°F, chills, tiredness, headaches or myalgia
[d] N is the number of vaccinated participants in the per-protocol analysis set for efficacy assessments
[e] n is the number of participants with protocol-defined influenza-like illness with laboratory confirmation
[f] Primary endpoint
[g] The pre-specified statistical superiority criterion for the primary endpoint (lower limit of the 2-sided 95% CI of the vaccine efficacy of Fluzone High-Dose relative to Fluzone > 9.1%) was met
[h] In the first year of the study the influenza B component of the vaccine and the majority of influenza B cases were of the Victoria lineage; in the second year the influenza B component of the vaccine and the majority of influenza B cases were of the Yamagata lineage

A secondary endpoint of the study was the occurrence of culture-confirmed influenza caused by viral types/subtypes antigenically similar to those contained in the respective annual vaccine formulations in association with a modified CDC-defined ILI, defined as the occurrence of a temperature >99.0°F (>37.2°C) with cough or sore throat. The efficacy of Fluzone High-Dose relative to Fluzone for this endpoint was 51.1% (95% CI: 16.8; 72.0).

REFERENCES

1. Lasky T, Terracciano GJ, Magder L, et al. The Guillain-Barré syndrome and the 1992-1993 and 1993-1994 influenza vaccines. *N Engl J Med* 1998;339:1797-1802. **2.** Baxter R, Bakshi N, Fireman B, et al. Lack of association of Guillain-Barré syndrome with vaccinations. *Clin Infect Dis* 2013;57:197-204.

HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Single-dose, prefilled syringe, without needle, 0.5 mL (NDC 49281-395-88) (not made with natural rubber latex). Supplied as package of 10 (NDC 49281-395-65).

Storage and Handling

Store Fluzone High-Dose refrigerated at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Discard if vaccine has been frozen. Do not use after the expiration date shown on the label.

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information). Inform the patient or caregiver that Fluzone High-Dose contains killed viruses and cannot cause influenza. Among persons aged 65 years and older, Fluzone High-Dose stimulates the immune system to produce antibodies that help protect against influenza. Among persons aged 65 years and older, Fluzone High-Dose offers better protection against influenza as compared to Fluzone. Annual influenza vaccination is recommended. Instruct vaccine recipients and caregivers to report adverse reactions to their healthcare provider and/or to Vaccine Adverse Event Reporting System (VAERS).

Fluzone is a registered trademark of Sanofi Pasteur Inc.

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Sanofi Pasteur Inc.
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MKT28980

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MONITORING

Although it may provide some benefit in certain patient populations, routine therapeutic drug monitoring is not recommended when caring for patients with HIV infection who are being treated with ART; however, monitoring for toxicity using laboratory testing is recommended. A patient's comorbidities and the ART regimen prescribed should be used to determine when and how often monitoring should occur in those patients who have received at least 16 weeks of treatment and who have not had any abnormal results; this monitoring should typically occur every three to six months.

After starting or modifying a patient's ART, HIV-1 RNA should be measured after four weeks. It should then be measured every three months to ensure that viremia is sufficiently suppressed. To guide plans for starting or stopping prophylaxis for opportunistic infection, a patient's CD4 cell count should be checked every three months, if not more often, after ART is started; this is particularly important in those with CD4 cell counts less than 200 per μL. In patients who are known to adhere to their ART regimen and who have an established CD4 cell count that remains at 350 per μL or higher and a suppressed HIV-1 RNA for one year, viral load and CD4 cell count only need to be evaluated every six months or less. Unless a patient has an immunosuppressive illness (for which the patient may or may not be receiving treatment) or there is virologic failure, CD4 cell counts do not have to be checked, unless desired, in those patients whose CD4 cell counts are consistently greater than 500 per μL and whose HIV-1 RNA has been suppressed for longer than two years.

Before making any conclusions about management in patients taking ART, physicians should ensure that each patient has an HIV-1 RNA level greater than 50 copies per mL on another sample taken within four weeks. If a patient's HIV-1 RNA level is greater than 200 copies per mL, physicians should determine what may have led to treatment failure and if switching the patient's regimen would help. Evaluating a patient's resistance to treatment using genotyping should occur in all patients who are treatment naive or for whom therapy has failed.

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