Discontinuation or Interruption of Antiretroviral Therapy

Updated: Jan. 20, 2022
Reviewed: Jan. 20, 2022

Discontinuation or interruption of antiretroviral therapy (ART) may result in viral rebound, immune decompensation, and/or clinical progression.[1-5] Thus, discontinuation or planned interruption of ART is not recommended outside the context of a clinical trial **(AI).** However, unplanned interruption of ART may occur under certain circumstances as discussed below.

Unanticipated Interruptions of Oral Antiretroviral Drugs

Reasons for short-term interruption (days to weeks) of ART vary and may include intercurrent illnesses that preclude oral intake (e.g., gastroenteritis, pancreatitis), surgical procedures, drug toxicity, or interrupted access to antiretroviral (ARV) drugs. Stopping ART for a short time (i.e., less than 1 day to 2 days) usually can be done by holding all drugs in the regimen. Whether unplanned interruptions occur by accident or by necessity (e.g., because of drug toxicities), all efforts should be made to minimize their duration. Recommendations for some specific scenarios are listed below.

When a Patient Experiences Unexpected Inability to Take Solid Oral Medications

For patients who require tube feeding, some ARV drugs are available in liquid formulations, and some pills may be crushed. The Oral Antiretroviral/HCV DAA Administration[6] provides information on crushing pills and formulating liquid ARV drugs. Additional information also may be available in drug product labels. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective ARV regimen.

For patients unable to take medications by any enteral route (e.g., in the context of severe gastrointestinal disease), all components of the oral drug regimen should be stopped simultaneously, regardless of half-lives of the drugs. After resolution, all components of the ARV regimen should be restarted simultaneously.

Several ARV drugs are available as parenteral formulations; these include zidovudine, enfuvirtide, ibalizumab (IBA), and the long-acting (LA) injectable formulations of cabotegravir (CAB LA) and rilpivirine (RPV LA). The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. However, this regimen has not been studied as an alternative for patients who cannot take oral medications. Clinicians should consult with an HIV specialist before prescribing any of these agents.

When a Patient Experiences a Severe or Life-Threatening Toxicity to an Antiretroviral Agent

All components of the ARV drug regimen should be stopped simultaneously, regardless of drug half-life. After resolution, a different complete regimen that does not include the offending agent should be started.

Interruption of Long-Acting Antiretroviral Drugs

The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. CAB LA and RPV LA are given as intramuscular (IM) injections and have extended half-lives. Therefore, patients who miss doses or discontinue therapy without bridging with an oral ARV regimen are at increased risk of virologic failure with development of drug resistance. Clinicians should refer to prescribing information for CAB LA and RPV LA for the management of missed doses or discontinuations.[7] For planned missed injection doses of CAB LA and RPV LA, oral formulations of CAB and RPV should be made available to patients as a bridging therapy for up to 2 months. Oral formulation of RPV is available by prescription in community pharmacies, but oral formulation of CAB is available only through the manufacturer. When stopping long-acting injectable ART, transition to a suppressive oral ARV regimen should occur within 4 weeks of the last planned IM doses. Patients who have missed or delayed clinic visits repeatedly should be reassessed to determine if resumption of injections is appropriate or if they may need to be transitioned back to an oral regimen. Plasma viral load testing should be performed before the transition, and drug-resistance testing should be considered if plasma viremia is present.

Patients with drug-resistant HIV may receive IBA as part of a salvage regimen. IBA is initiated with a 2,000-mg loading dose given as an intravenous (IV) infusion, then followed by 800 mg given as an IV infusion every 14 days as maintenance therapy. If a dose is missed by ≥3 days, a repeat loading dose of 2,000 mg IV infusion is recommended before resumption of maintenance therapy.

Analytical Treatment Interruption

Several research studies are evaluating approaches to achieve sustained ART-free viral remission or a functional cure for HIV.[8] Viral eradication (i.e., elimination of HIV entirely from an individual) remains a more challenging, longer-term goal. Currently, the only way to reliably test the effectiveness of these strategies is to interrupt ART and closely monitor for viral rebound in the setting of a clinical trial, an approach referred to as "analytical treatment interruption" or ATI.[9] The duration of treatment interruption, the dynamics of viral rebound, and the criteria for restarting ART are part of ATI clinical trial designs with the goal to conduct these clinical trials safely.

Before ART is interrupted, participants of ATI trials should be made aware of and understand the risks of viral rebound,[10] acute retroviral syndrome, increased risk of HIV transmission, decline of CD4 count, HIV disease progression, development of minor HIV-associated manifestations (e.g., oral thrush) or serious non-AIDS complications (e.g., renal, cardiac, hepatic, or neurologic complications), and the development of drug resistance. Patients should be counseled about the need for close clinical and laboratory monitoring during ART interruptions and provided counseling and linkage to pre-exposure prophylaxis services should they wish to refer sexual partners at risk for acquiring HIV.

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