Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

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What Not to Use *(Last updated October 17, 2017; last reviewed October 17, 2017)*

Some antiretroviral (ARV) regimens or components are not generally recommended because of suboptimal antiviral potency, unacceptable toxicities, or pharmacologic concerns. These are summarized below.

**Antiretroviral Drugs Not Recommended**

The following ARV drugs are no longer recommended for use because of suboptimal antiviral potency, unacceptable toxicities, high pill burden, or pharmacologic concerns: delavirdine (DLV), didanosine (ddI), indinavir (IDV), nelfinavir (NFV), and stavudine (d4T).

**Antiretroviral Regimens Not Recommended**

**Monotherapy**

Nucleoside reverse transcriptase inhibitor (NRTI) monotherapy is inferior to dual-NRTI therapy.¹ Protease inhibitor (PI) monotherapy is inferior to combination antiretroviral therapy (ART).²⁻⁶ Integrase strand transfer inhibitor (INSTI) monotherapy has resulted in virologic rebound and INSTI resistance (AI).⁷,⁸

**Dual-NRTI Regimens**

These regimens are inferior to triple-drug combination regimens (AI).⁹

**Triple-NRTI Regimens**

Triple-NRTI regimens have suboptimal virologic activity¹⁰⁻¹² or a lack of data (AI).

**Antiretroviral Components Not Recommended**

**Atazanavir plus Indinavir**

Both PIs can cause Grade 3 to 4 hyperbilirubinemia and jaundice. Additive adverse effects may be possible when these agents are used concomitantly (AIII).

**Cobicistat plus Ritonavir as Pharmacokinetic Enhancers**

This combination may be prescribed inadvertently, which may result in additive CYP3A4 enzyme inhibition and may further increase the concentrations of ARV drugs or other concomitant medications (see Tables 18a and 18d).

**Didanosine plus Stavudine**

The combination of ddI and d4T can result in peripheral neuropathy, pancreatitis, and lactic acidosis, and it has been implicated in the deaths of several pregnant women (AII).¹³

**Didanosine plus Tenofovir Disoproxil Fumarate**

Tenofovir disoproxil fumarate (TDF) increases ddI concentrations,¹⁴ serious ddI-associated toxicities,¹⁵,¹⁶ immunologic nonresponse,¹⁷ early virologic failure,¹⁸,¹⁹ and resistance¹⁸,²⁰ (AII).

**Two Non-Nucleoside Reverse Transcriptase Inhibitor Combinations**

Excess clinical adverse events and treatment discontinuation were reported in patients randomized to receive treatment with two non-nucleoside reverse transcriptase inhibitors (NNRTIs).²¹ Efavirenz (EFV) and nevirapine (NVP) are enzyme inducers, and both of these drugs can reduce concentrations of etravirine (ETR) and rilpivirine (RPV) (AI).²²
Emtricitabine plus Lamivudine
Both drugs have similar resistance profiles and have minimal additive antiviral activity. Inhibition of intracellular phosphorylation may occur in vivo (AIII).²³

Etravirine plus Unboosted Protease Inhibitor
ETR may induce the metabolism and significantly reduce the drug exposure of unboosted PIs. Appropriate doses of the PIs have not been established (AII).²²

Etravirine plus Fosamprenavir/Ritonavir
ETR may alter the concentrations of these PIs. Appropriate doses of the PIs have not been established (AII).²²

Etravirine plus Tipranavir/Ritonavir
Tipranavir/ritonavir (TPV/r) significantly reduces ETR concentrations (AII).²²

Nevirapine Initiated in ARV-Naive Women with CD4 Counts >250 cells/mm³ or in ARV-Naive Men with CD4 Counts >400 cells/mm³
Initiating NVP below these CD4 count thresholds increases the risk of symptomatic, and sometimes life-threatening, hepatic events.²⁴-²⁶ Patients with CD4 counts above these thresholds due to ART can safely switch to NVP (BI).²⁷

Unboosted Darunavir, Saquinavir, or Tipranavir
The virologic benefit of these PIs has been demonstrated only when they were used with concomitant RTV, or in the case of DRV, also with COBI (AII).

Stavudine plus Zidovudine
These NRTIs are antagonistic in vitro²⁸ and in vivo²⁹ (AII).

Tenofovir Alafenamide plus Tenofovir Disoproxil Fumarate
This combination may be prescribed inadvertently, especially during transition from one formulation to another. There is no data supporting any potential additive efficacy or toxicity if TAF and TDF are used in combination.

References


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