Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents 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 21a and 21d).

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 \textit{in vivo} (AIII).\textsuperscript{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).\textsuperscript{22}

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

**Etravirine plus Tipranavir/Ritonavir**
Tipranavir/ritonavir (TPV/r) significantly reduces ETR concentrations (AII).\textsuperscript{22}

**Nevirapine Initiated in ARV-Naive Women with CD4 Counts >250 cells/mm\textsuperscript{3} or in ARV-Naive Men with CD4 Counts >400 cells/mm\textsuperscript{3}**
Initiating NVP in ART-naive individuals with CD4 counts above these thresholds increases the risk of symptomatic, and sometimes life-threatening, hepatic events.\textsuperscript{24-26} ART-experienced patients can safely switch to NVP if they have CD4 counts above these thresholds as a result of receiving effective ART (BI).\textsuperscript{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 \textit{in vitro}\textsuperscript{28} and \textit{in vivo}\textsuperscript{29} (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**


