

SELECTION OF THE INITIAL HAART REGIMEN

The optimal HAART regimen provides potency and durability with a simple dosing schedule and minimal adverse effects while preserving future treatment options in the event of treatment failure. Fortunately, the introduction of additional ARV agents and the development of combination pills over the past several years have resulted in a number of potent therapeutic options that are simpler and better tolerated than earlier HAART regimens.

PI-Based vs. NNRTI-Based vs. Triple-NRTI Regimens

Initial HAART regimens typically consist of a combination of two NRTIs (the *nucleoside backbone*) plus an NNRTI or a PI (which may or may not be boosted by low doses of RTV¹). HAART regimens consisting of a dual nucleoside backbone plus an NNRTI can be described as *NNRTI-based* regimens, whereas *PI-based* regimens consist of a dual nucleoside backbone plus a PI (sometimes boosted by RTV¹). Either PI-based or NNRTI-based regimens are reasonable options for initial HAART; each has distinct advantages and disadvantages (see *Table 5*). HAART regimens consisting of three NRTIs (*triple NRTI regimens*) such as AZT plus 3TC plus ABC can also be considered for initial therapy, but are not generally recommended unless significant contra-indications exist to more potent conventional PI- or NNRTI-based regimens. Triple NRTI combinations that include TDF plus ABC or TDF plus ddI appear to perform particularly poorly and should be avoided.

For most patients in the Caribbean region, the advantages of an NNRTI-based initial HAART regimen outweigh those of a PI-based regimen, chiefly due to the simplicity of these regimens (low pill burden, once- or twice-daily dosing schedule without significant food restrictions, no refrigeration requirements); a wide availability of NVP and EFV (including combination tablets for NVP); generally favourable tolerability; and potency.

Table 5: Advantages and Disadvantages of Different Types of HAART Regimens

REGIMEN TYPE EXAMPLES	ADVANTAGES	DISADVANTAGES
NNRTI-based <ul style="list-style-type: none"> • 2 NRTIs + NVP • 2 NRTIs + EFV 	<ul style="list-style-type: none"> • Low pill burden • Simple dosing schedule • Few food restrictions • No refrigeration requirements • Fewer metabolic complications than PI-based regimens² • Preserves PI options for future regimens 	<ul style="list-style-type: none"> • Low genetic barrier to resistance³ • Cross-resistance among NNRTIs⁴ • Potential for hepatic and skin toxicity (NVP>EFV) • Potential teratogenicity (EFV)⁵ • High potential for interactions with other medications
PI-based <ul style="list-style-type: none"> • 2 NRTIs + LPV/r • 2 NRTIs + NFV 	<ul style="list-style-type: none"> • Longest prospective study data demonstrating survival benefit • Preserves NNRTI options for future regimens • High genetic barrier to resistance⁶ 	<ul style="list-style-type: none"> • Higher pill burden • Gastrointestinal side effects common • Metabolic complications common • Refrigeration requirements for some agents (RTV, LPV/r)⁷ • High potential for interactions with other medications
Triple NRTI <ul style="list-style-type: none"> • AZT + 3TC + ABC • d4T + 3TC + ABC 	<ul style="list-style-type: none"> • Simple dosing • Low pill burden • Low potential for metabolic complications • Low potential for interactions with other medications 	<ul style="list-style-type: none"> • Lower potency/higher rates of clinical failure than EFV-based regimens • Potential for ABC hypersensitivity

¹See *Appendix B* for background and dosing information regarding the use of low-dose RTV to boost serum levels of other PIs.

²Dyslipidaemia, insulin resistance, and possibly lipodystrophy are metabolic complications of HAART most commonly associated with PI-based regimens, though they may also be seen with NNRTI-based regimens as well.

³A single point mutation in HIV reverse transcriptase can confer complete resistance to the NNRTI class. See *Appendix F* for more information regarding HIV resistance.

⁴Resistance to EFV typically confers resistance to NVP and *vice versa*.

⁵Severe neurological birth defects have been documented in the offspring of non-human primates exposed to EFV during pregnancy.

⁶Clinically significant resistance to most PIs requires multiple mutations. See *Appendix F* for more information regarding HIV resistance.

⁷RTV should be stored at 2° to 8°C (36° to 46°F) prior to dispensing. After dispensing, it can be stored at room temperature (defined as less than 25°C, or 77°F) as long as it is used within thirty days (Source: Norvir® (ritonavir) package insert. Abbott Park, Ill: Abbott Pharmaceuticals).