Adult ART Table 1. When to Start Therapy*			
Clinical Category	**CD4+ Count**	**Viral Load**	**Recommendation**
Symptomatic (AIDS or severe symptoms)	Any value	Any value	Treat
Asymptomatic, AIDS	CD4+ < 200/mm^3	Any value	Treat
Asymptomatic	CD4+ > 200/mm^3 but < 350/mm^3	Any value	Offer treatment, but consider patient readiness, probability of adherence, potential side effects, and prognosis based on CD4 count, CD4 slope, and HIV viral load
Asymptomatic	CD4+ > 350/mm^3	> 100,000 c/mL	Consider therapy or observe (Data inconclusive for either alternative)
Asymptomatic	CD4+ > 350/mm^3	< 100,000 c/mL	Defer therapy and observe

* There are special considerations for pregnant women; consult Pregnancy Tables 1-3

Adult ART Table 2. Suggested Minimum Target Trough Levels	
Drug	**Concentration**
APV	400 mg/mL
IDV	100 mg/mL
LPV	1000 mg/mL
NFV	800 mg/mL
RTV	2100 mg/mL
SQV	100-250 mg/mL
EFV	1000 mg/mL
NVP	3400 mg/mL

Adult ART Table 3. Starting Regimens for Antiretroviral Naïve Patients		
NRTI-Based Regimens		**# of pills per day**
Preferred Regimens	efavirenz + (lamivudine or emtricitabine) + (zidovudine or tenofovir DF) – except for pregnant women or women with pregnancy potential	2–3
Alternative Regimens	• efavirenz + (lamivudine or emtricitabine) + (didanosine or stavudine or abacavir) - except for pregnant women or women with pregnancy potential	2–4
	• nevirapine + (lamivudine or emtracitabine) +(zidovudine or abacavir or tenofovir or stavudine* or didanosine) (Avoid in women with baseline CD4>250 and men with baseline CD4 > 400)	3–6
PI-Based Regimens		**# of pills per day**
Preferred Regimens	lopinavir/ritonavir + (lamivudine or emtricitabine) + zidovudine	6–7
Alternative Regimens	• atazanavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or abacavir or didanosine) or (tenofovir + ritonavir)	3–6
	• fosamprenavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or abacavir or tenofovir or didanosine)	5–8
	• fosamprenavir/ritonavir + (lamivudine or emtricitabine) + (zidovudine or tenofovir or didanosine or stavudine* or abacavir)	5–8
	• indinavir + ritonavir† + (lamivudine or emtricitabine) + (zidovudine or tenofovir or didanosine or stavudine* or abacavir)	7–12
	• nelfinavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or tenofovir or didanosine or abacavir)	5–8
	• saquinavir (Invirase) + ritonavir + (lamivudine or emtricitabine) + (zidovudine or stavudine* or tenofovir or didanosine or abacavir)	7-15
	• lopinavir/ritonavir + (lamivudine or emtricitabine) + (stavudine* or abacavir or tenofovir or didanosine)	5-7
Triple NRTI Regimen – As Alternative to PI- or NNRTI-based regimens		**# of pills per day**
Alternative Regimens	• abacavir + lamivudine + zidovudine	2

* Stavudine is associated with higher rates of lipoatrophy and mitochondrial toxicity than other NRTIs
† Low-dose (100-400 mg) ritonavir

Adult ART Table 4.
Advantages and Disadvantages of Antiretroviral Regimens

	Advantages	Disadvantages
NNRTIs	**Class– less lipodystrophy Save PI option Extensive experience**	**Low genetic barrier to resistance Class resistance / Drug interactions High rate of rash reactions**
EFV	Potent Low pill burden qd Once daily dosing	CNS toxicity Teratogenic in first trimester
NVP	Extensive experience in pregnancy No food effect	ADR: hepatotoxicity + rash Contraindicated in women with baseline CD4 count >250
PI	**Class– extensive experience Save NNRTI option**	**ADR– lipodystrophy Multiple drug interactions GI intolerance**
ATV	Once daily dosing Low pill burden No hyperlipidemia	ADR: Jaundice + PR interval prolongation Drug interaction with TDF and EFV
LPV/r	Potency Coformulated with RTV	ADR: GI intolerance Reduced levels in pregnancy
FPV/r	Low pill burden No food effect Once daily dosing	ADR: skin rash
IDV/r	No food requirement bid dosing with RTV boosting	ADR: Nephrolithisis Requirement for po fluid
NFV	Substantial experience in pregnancy	ADR: diarrhea High rate virologic failure Food requirement
SQV/r	Improved GI tolerance with Invirase	ADR: GI intolerance
NRTIs		
AZT/ 3TC/ ABC	Coformulated No food effect Preserves PI and NNRTI options	Higher rate of virologic failure if used alone ADR: ABC hypersensitivity
NRTI pairs		
AZT/ 3TC*	Extensive experience Coformulated No food effect	ADR: GI intolerance + narrow suppression (AZT) HBV flare when 3TC stopped
d4T/ 3TC*	No food effect Once daily	ADR of d4T ** HBV flare when 3TC stopped
TDF/ 3TC* or FTC	Well tolerated Once daily TDF + FTC coformulated	HBV flare when TDF, 3TC, or FTC stopped
ddI/ 3TC*	Once daily	ADR: ddI** Food effect HBV flare when 3TC stopped
ABC/ 3TC*	Once daily No food effect Coformulated	ADR: ABC hypersensitivity HBV flare when 3TC stopped

* FTC is similar to 3TC; has longer intracellular half life and has less extensive experience

** ADRs- d4T lipoatrophy, lactic acidosis, peripheral neuropathy; ddI- peripheral neuropathy, pancreatitis and lactic acidosis

Adult ART Table 5. Antiretroviral Regimens or Components That Are Not Generally Recommended		
	Rationale	**Exception**
Antiretroviral Regimens Not Recommended		
Monotherapy	• Rapid development of resistance • Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	Pregnant women with HIV-RNA <1,000 copies/mL using zidovudine monotherapy for prevention of perinatal HIV transmission
Two-agent drug combinations	• Rapid development of resistance • Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	For patients currently on this treatment, it may be reasonable to continue if virologic goals are achieved
ABC + TDF + 3TC as a triple NRTI regimen	High rate of virologic failure and resistance	No exception
TDF + ddI + 3TC	High rate of virologic failure and resistance	No exception
TDF + ddI + NNRTI	High rate of virologic failure Possible reduced CD4 response	No exception
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Saquinavir hard gel capsule (Invirase) as single PI	• Poor oral bioavailability (4%) • Inferior antiretroviral activity when compared to other protease inhibitors	No exception
d4T + ddI	Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis	When no other antiretroviral options are available and potential benefits outweigh the risks*
ATV + IDV	Potential for additive hyperbilirubinemia	No exception
FTC + 3TC	No potential benefit	No exception
Efavirenz in pregnancy	Teratogenic in nonhuman primate	When no other antiretroviral options are available and potential benefits outweigh the risks*

Adult ART Table 5. – *continued* Antiretroviral Regimens or Components That Are Not Generally Recommended		
	Rationale	**Exception**
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen *(continued)*		
Amprenavir oral solution in: • pregnant women • children <4 yr old • patients with renal or hepatic failure • patients treated with metronidazole or disulfiram	Oral liquid contains large amount of the excipient propylene glycol, which may be toxic in the patients at risk	No exception
d4T + ZDV	Antagonistic	No exception
ddC + d4T or ddC + ddI	Additive peripheral neuropathy	No exception
ATV + IDV	Additive hyperbilirubinemia	No exception
FTC + 3TC	Similar agents; no potential benefit	No exception
Hydroxyurea	• Decreases CD4 count • Augments d4T- and ddI-associated side effects, such as pancreatitis & peripheral neuropathy • Inconsistent evidence of improved viral suppression • Contraindicated in pregnancy (Pregnancy Category D)	No exception
Not Recommended As Part of Initial Antiretroviral Regimen		
DLV	Modest antiretroviral effect	*
RTV as single PI	GI intolerance	*
d4T + ddI	Increased peripheral neuropathy, lactic acidosis, and pancreatitis	*
NFV + SQV	High pill burden of 16-22 caps/day	*
TPV	Tested and approved only for salvage	*

* Reasonable to use in unusual circumstances

Adult ART Table 6.
Laboratory Monitoring

- Baseline tests, CBC, chemistry profile including liver and renal function tests, PAP smear for female patients, *Toxoplasma gondii* IgG, VDRL (or RPR), anti-HCV, anti-HBc, and PPD (if no prior positive, see TB tables)
- Confirm HIV Ab + if not documented
- Viral load at baseline (x2) and 2-8 wks after initiating therapy or new regimen, then every 3-4 months, clinical event, or significant (3x or > 0.5 log10 c/mL) change in VL
- CD4 count at baseline and then every 3-6 months
- Antiretroviral agent toxicity (see Drug Table 2, pg 8)
- Resistance tests

  Recommended
  - Virologic failure within 4 weeks of stopping ART
  - Suboptimal suppression
  - Acute HIV infection

  Consider
  - Chronic HIV infection, before therapy

  Not Usually Recommended
  - After discontinuation of drugs for more than 4 weeks
  - Viral load < 1,000 c/mL

Adult ART Table 7. Resistance Mutations*		
Drug	**Major †**	**Minor †**
Protease Inhibitors		
IDV	46 IL, 82 AFT, 84 V	10 IRV, 20 MR, 24 I, 32 I, 36 I, 54 V, 71 VI, 73 SA, 77 I, 90 M
NFV	30 N, 90 M	10 FI, 36 I, 46 IL, 71 VL, 77 I, 82 AFTS, 84 V, 88 DS
RTV	82 AFTS, 84 V	10 FIRV, 20 MR, 32 I, 33 F, 36 I, 46 IL, 50 V, 54 VL, 71 VT, 77 T, 90 M
SQV	48 V, 90 M	10 IRV, 54 VL, 71 VT, 73 S, 77 I, 82 A, 84 V
FPV	50 V, 84 V	10 FIRV, 32 I, 46 IL, 47 V, 54 LVM, 73 S, 82 AFST,90 M
LPV/r	32 I, 47 VA, 82 AFTS	10 FIVR, 20 MR, 24 I, 31 I, 33 F, 46 IL, 50 V, 53 L, 54 VLAMTS, 63 P, 71 VT, 73 S, 90 M
ATV	50 L, 84 V, 88 S	10 IFV, 16 E, 20 RMI, 24 I, 32 I, 33 IFV, 36 ILV, 46 I, 48 V, 54 LVMT, 60 E, 62 V, 71 VITL, 73 CSTA, 82 A, 90 M, 93 L
TPV	33 I, 82 LT, 84 V	10 IV, 13 V, 20 MR, 35 G, 36 I, 43 T, 46 L, 47 V, 54 AMV, 58 E, 69 K, 74 P, 83 D, 90 M, 46 I, 54 V

* Adapted from IAS-USA Topics HIV Med 2005; 13:125. See http://www.iasusa.org

† **Major**: usually develop first; associated with decreased drug binding; **Minor**: also contribute to drug resistance; may affect drug binding in vitro less than primary mutations. Use of **Major** and **Minor** designations for NRTIs and NNRTIs has been suspended.

Adult ART Table 7. – *continued* Resistance Mutations*	
Drug	**Codon Mutations**
Nucleosides and Nucleotides	
AZT	41 L, 44 D, 67 N, 70 R, 118 I, 210 W, 215 YF, 219 Q
d4T	41 L, 44 D, 65 R, 67 N, 70 R, 118 I, 210 W, 215 YF, 219 QE
3TC	65 R, 184 VI
FTC	65 R, 184 VI
ddI	65 R, 74 V
ABC	65 R, 74 V, 115 F, 184 V
TDF	65 R
Multinucleoside A- Q 151 M	62 V, 75 I, 77 L, 116 Y, 151 M
Multinucleoside B 69 insertion	41 L, 67 N, 69 insert, 70 R, 210 W, 215 YF, 219 QE
Multinucleoside TAMS	41 L, 67 N, 70 R, 210 W, 215 YF, 219 QE
NNRTIs	
NVP	100 I, 103 N, 106 AM, 108 I, 181 CI, 188 CLH, 190 A
DLV	103 N, 106 M, 181 C, 188 L, 236 L
EFV	100 I, 103 N, 106 M, 108 I, 181 CI, 188 L, 190 SA, 225 H
Multi-NNRTI resistance	103 N, 106 M, 188 L
Multi-NNRTI resistance-accumulation	100 I, 106 A, 181 CI, 190 SA, 230 L

* Adapted from IAS-USA Topics HIV Med 2005; 13:125. See http://www.iasusa.org

Therapeutic Failure

Definitions

Virologic Failure:

- Failure to achieve VL < 400 c/mL by 24 wks or < 50 c/mL by 48 wks. Note: Most patients will have a decrease in VL of ≥1 $\log_{10}$ c/mL at 1–4 weeks
- Viral suppression followed by repeated positive viral load

Immunologic Failure:

Failure to increase CD4 count 25-50 cells/mm^3 during first year
Note: Mean increase is about 150 cells/mm^3 in a year with HAART in treatment naïve patients

Clinical Failure:

Occurrence or recurrence of HIV-related event ≥ 3 months after start of HAART

Note: Must exclude immune reconstitution syndromes

Management of Regimen Failure

Assessment

- Adherence: Address cause and/or simplify regimen
- Tolerability
  - Change one drug within class
  - Change classes; e.g. PI-based HAART vs NNRTI-based HAART
- Pharmacokinetic Issues

Therapeutic Failure – *continued*

Virologic Failure

Definition:

1) HIV RNA > 400 c/mL (VL) after 24 weeks of treatment

2) VL > 50 c/mL after 48 weeks of treatment

3) Viral load detectable after achieving undetectable (viral rebound) VL indicating failure should be confirmed; "Blips" (isolated VL values of 50–1,000 c/mL) do not constitute failure if unconfirmed

Assessment:

- Review treatment history and prior resistance tests
- Access adherence, intolerance and pharmacokinetic issues (food/fasting requirements, drug interactions, malabsorption)
- Distinguish between limited, intermediate, and extensive prior treatment and drug resistance
- The viral load that defines an indication for therapeutic intervention is in the range of 400–5000 c/mL; The threshold of 400 may result in multiple drug exposures and limited access to resistance tests (since a threshold of 1000 c/mL is often required to do the test); a delay to a threshold of 5000 c/mL risks accumulation of multiple resistance mutations including class resistance
- Perform resistance tests while the patient is receiving the failed regimen or within 4 weeks of stopping it
- Identify 2–3 active drugs for the next regimen; two active drugs are essential for viral supression
- If no resistance is demonstrated: consider continuation with emphasis on adherence, possibly with therapeutic drug monitoring
- With low level viremia (< 5000 c/mL) and limited drug exposure consider boosting a PI, or intensification by adding a nucleoside or change therapy
- With intermediate or extensive prior drug exposure, consider an agent with a new mechanism of action (enfuvertide) usually combined with a PI including TPV or an experimental drug such as TMC 114
- With extensive treatment failures, multiple resistance mutations and no available regimens likely to achieve virologic goals: the goal of therapy is to preserve immune function and avoid HIV-associated complications; HIV therapy should be continued

Adult ART Table 8.
Methods to Achieve Readiness to Start HAART & Maintain Adherence

Patient-related

- Negotiate a plan or regimen that the patient understands and to which she or he commits
- Take time needed, > 2 visits, to ensure readiness before 1st prescription
- Recruit family, friends, peer and community support
- Use memory aids: timers, pagers, written schedule, pill boxes/ medication organizers
- Plan ahead: keep extra meds in key locations, obtain refills
- Use missed doses as opportunities to prevent future misses
- Active drug and alcohol use and mental illness predict poor adherence; race, sex, age, educational level, income, and past drug use do not

Provider/Health Team-related

- Educate patient re: goals of therapy, pills, food effects, and side effects
- Assess adherence potential before HAART; monitor at each visit
- Ensure access at off-hours and weekends for answering questions or addressing problems
- Utilize full health care team; ensure med refills at pharmacy
- Consider impact of new diagnoses and events on adherence
- Provide training updates on adherence for all team members and utilize team to reinforce adherence
- Monitor adherence and intensify management in periods of low adherence
- Educate volunteers, patient-community representatives

Regimen-related

- Avoid adverse drug interactions
- Simplify regimen re: dose frequency, pill burden, and food requirements
- Inform patient about side effects
- Anticipate and treat side effects

Adult ART Table 9.
National Cholesterol Education Program:
Indications for Dietary or Drug Therapy for Hyperlipidemia

Coronary Heart Disease Risk Status	Goal	Threshold for Diet Rx	Threshold for Drug Rx
No CHD & 0-1 Risks*	LDL <160 mg/dL	LDL ≥160 mg/dL	LDL >190 mg/dL (LDL 160-190 Drug therapy optional)
No CHD & ≥ 2 Risks*	LDL <100 mg/dL	LDL ≥130 mg/dL	10 Yr CHD Risk <10% ‡ LDL > 160 mg/dL
			10 Yr CHD Risk 10-20% ‡ LDL >130 mg/dL
CHD or CHD equivalent: • Clinical ASCVD † • Diabetes mellitus • Multiple Risk Factors conferring 10 Yr risk of CHD of >20% ‡	LDL < 70 mg/dL	LDL ≥100 mg/dL	LDL >130 mg/dL (100-129 mg/dL: drug optional)

Triglycerides are an independent consideration

- For patients with serum triglycerides >500 mg/dL the primary goal is reduction of triglycerides to prevent pancreatitis and reduce risk of CHD
- For patients with serum triglycerides 200 - 499 mg/dL reduction of non-HDL cholesterol becomes a secondary goal after reaching LDL goal

Adapted from: JAMA 2001; 285:2486-2497; updated NCEP – *Circulation* 2004; 110:227.

Editors Note: This table is a basic condensation of complex guidelines. Readers are encouraged to consult and use the tools available on the NHLBI web site: http://www.nhlbi.nih.gov/guidelines/cholesterol/

* CHD Risk Factors: Age (men >45 years; women >55 yrs or premature menopause without estrogen replacement); hypertension, current smoking, history of cardiovascular disease in first degree relative (<55 years for male relative and <65 years for female relative), or serum HDL cholesterol <40 mg/dL. If high HDL (>60 mg/dL) subtract one risk factor.

† Atherosclerotic cardiovascular disease (ASCVD) includes peripheral artery disease, symptomatic carotid artery disease, and abdominal aortic aneurysm.

‡ Calculation of 10 year risk of CHD requires tables which may be found in the JAMA 2001;285:2486 or the NHLBI website: http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm

Adult ART Table 10.
Drug Therapy for Hyperlipidemia

(Recommendations of the ACTG [Dube MP et al, CID 2000; 31:1216])

Lipid Problem	Preferred	Alternative	Comment
Isolated high LDL	Statin*	Fibrate†	Start low doses and titrate up; with PIs watch for myopathy
High cholesterol and triglycerides	Statin* or fibrate†	Start one and add other	Combination may increase risk of myopathy
Isolated high triglycerides	Fibrate†	Statin*	Combination may increase risk of myopathy

NOTE:

Optimal management of hyperlipidemia should begin with specific risk factor reduction interventions such as: low-fat diet; regular exercise; moderation of alcohol intake; smoking cessation, blood pressure control, and diabetes control (where applicable). The likelihood of success with drug therapy for hyperlipidemia is substantially reduced in the absence of such interventions.

* Statin: Pravastatin 20 mg/day (max. 40 mg/day), fluvastatin 20-40 mg/day, or atorvastatin 10 mg/day. Use particular caution when giving LPV/r or NFV with Atorvastatin; also see Table 5. Drug Interactions: Contraindicated Combinations.

† Fibrate: Gemfibrozil 600 mg bid ≥ 30 minutes before meal or Fenofibrate tablets (e.g. Tricor) 160 mg qd Micronized fenofibrate (capsules) 67mg qd to start, max. dose 201 mg qd