Treatment Guidelines for ART-Naïve Patients

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Conflict of Interest Disclosure Statement

- The presenter has no conflicts to declare.

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Learning Objectives

1. List preferred regimens for treatment naïve patients.
2. List baseline labs that should be ordered prior to treatment initiation.
3. Recognize the pros/cons of each of the recommended regimens.

When to Start ART

- ART is recommended for treatment:
  - "ART is recommended for all HIV-infected individuals, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection." (A1)
  - The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV **(AII)**
- ART is recommended for prevention:
  - "ART also is recommended for HIV-infected individuals to prevent HIV transmission." (A1)

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

Recommendations for Initiating ART: Considerations

- ART should be initiated immediately after diagnosis
  - On a case-by-case basis, ART may be deferred because of clinical and/or psychological factors
- Patients should understand that indefinite treatment is required; ART does not cure HIV
- Address strategies to optimize care engagement and treatment adherence

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

Baseline Data

- CD4 count (AI)
  - Used to stage disease; Immune function assessment
  - Assess if opportunistic infection (OI) prophylaxis is needed
- HIV viral load (AI)
  - May help provider decide on regimen
  - Gauge treatment efficacy & adherence
- Complete blood count, chemistry profile, transaminase levels, blood urea nitrogen (BUN), and creatinine, urinalysis, and serologies for hepatitis A, B, and C viruses (AIII)
- Fasting blood glucose & Lipid panel (AIII)
- Genotype-test for resistance (BII)

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

Baseline Data

- Screening for STIs
- Toxoplasma IgG
- HLA-B5701: necessary if considering abacavir
- Current medication list-to check for potential drug interactions
- Comorbidities (including opportunistic infections), pregnancy test
- Evaluation of the patient's readiness for ART
  - assessment of high-risk behaviors, substance abuse, social support, mental illness, comorbidities, economic factors (e.g., unstable housing), medical insurance status and adequacy of coverage

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

Current ARV Medications

NRTI

- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Tenofovir DF (TDF)
- Tenofovir alafenamide (TAF)
- Zidovudine (AZT, ZDV)

NNRTI

- Doravirine (DOR)
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)

Attachment Inhibitor

- Fostemsavir (Rukobia®)

PI (require boosting)

- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Lopinavir (LPV)
- Saquinavir (SQV)
- Tipranavir (TPV)

Integrase Inhibitor (INSTI)

- Dolutegravir (DTG)
- Elvitegravir (EVG)
- Raltegravir (RAL)
- Bictegravir (BIC)

Fusion Inhibitor

- Enfuvirtide (ENF)

CCR5 Antagonist

- Maraviroc (MVC)

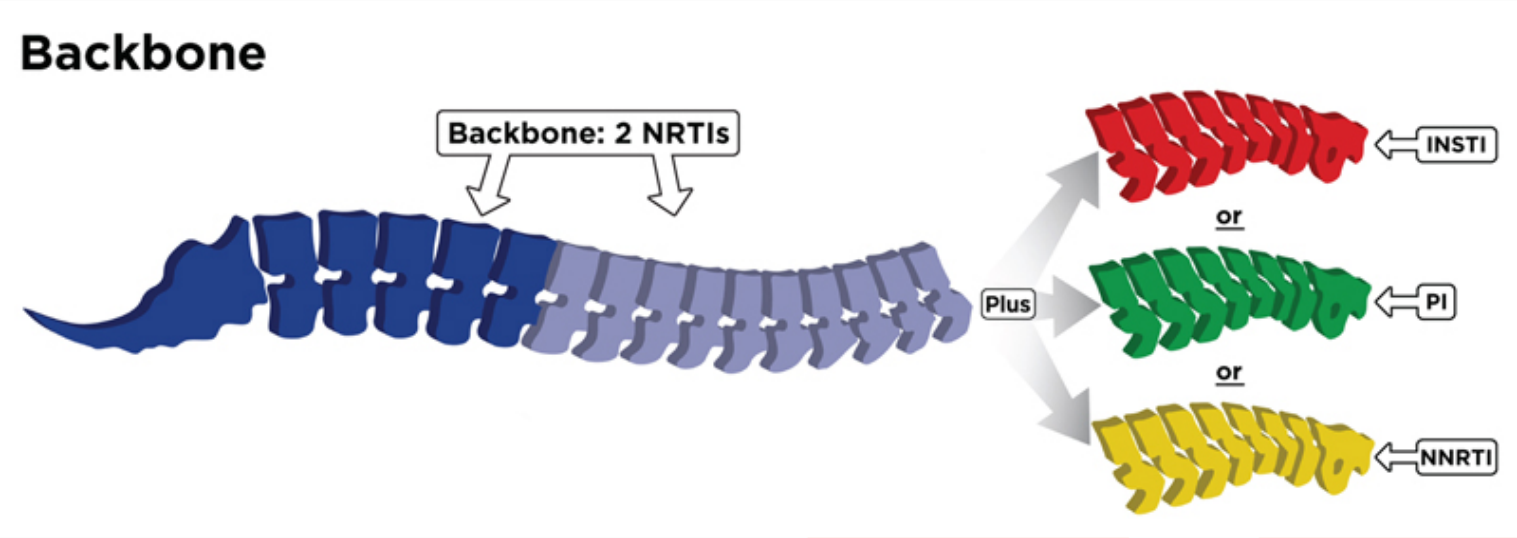
Post-Attachment Inhibitor

- Ibalizumab

Pharmacokinetic Booster

- Ritonavir (RTV)
- Cobicistat (COBI)

HAART Guidelines Initial Regimen



DHHS *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents.* https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0

Preferred NRTI Backbone Choices

- Tenofovir DF + emtricitabine

OR

- Tenofovir DF + lamivudine

OR

- Tenofovir alafenamide (TAF) + emtricitabine

OR

- Abacavir + lamivudine
  only as part of ABC/3TC/dolutegravir

Renal function, bone density concerns

Only if HLA B5701 absent

Modified from original slide by Kate Morton, PharmD

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent/0/

Initial Regimens: Recommended

Recommended Initial Regimens for Most People with HIV	**INSTI plus 2 NRTIs:** BIC/TAF/FTC **(AI)**[a] DTG/ABC/3TC **(AI)—if HLA-B*5701 negative** DTG plus (TAF or TDF)[a] plus (FTC or 3TC) **(AI)** **INSTI plus 1 NRTI:** DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Recent studies have shown that the prevalence of infant NTDs associated with DTG exposure at conception is slightly higher than with non-DTG containing regimens (1.9 per 1,000 versus 1.1 per 1,000, respectively), but the prevalence difference was not statistically significant

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive?view=full

Initial Regimens: Alternative

NNRTI based	DOR/TDF[c]/3TC **(BI)** or DOR plus TAF[c]/FTC **(BIII)** EFV plus (TAF or TDF)[c] plus (FTC or 3TC) EFV 600 mg plus TDF plus (FTC or 3TC) **(BI)** EFV 400 mg/TDF/3TC **(BI)** EFV 600 mg plus TAF/FTC **(BII)** RPV/(TAF or TDF)[c]/FTC **(BII for TAF and BI for TDF)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3**
PI based	(DRV/c[b] or DRV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(AI)**[b] (ATV/c[b] or ATV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(BI)**[b] (DRV/c[b] or DRV/r) plus ABC/3TC —**if HLA-B*5701 negative (BII)**[b]
INSTI based	EVG/c/(TAF or TDF)a/FTC **(BI)**[b] RAL plus (TAF or TDF)[a] plus (FTC or 3TC) **(BI for TDF/[FTC or 3TC], BII for TAF/FTC)**

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive?view=full

Alternative Regimens When NRTI Cannot Be used

NRTI-sparing	DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available DRV/r plus RAL twice a day **(CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3** DRV/r once daily plus 3TC[a] **(CI)**

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive?view=full

Considerations Prior to Rx HAART

- Comorbid conditions: renal disease, liver disease (cirrhosis, HBV, HCV), osteoporosis, pregnancy, cardiovascular diseases, psychiatric illness, TB
- Drug absorption: i.e. acidic stomach, chelators, food requirement
  - Can be Taken Without Regard to Food: BIC-, DOR-, DTG-, or RAL-based regimens
  - Should be Taken with Food: ATV/r- or ATV/c-, DRV/r- or DRV/c-based regimens, EVG/c/(TAF or TDF)/FTC, RPV-based regimens
  - Should be Taken on an Empty Stomach: EFV-based regimens
- Drug interactions: need current medication list
- Insurance/formulary
- Patient preference: pill count, food requirement, dosing frequency, likelihood of adherence

Drug Specific Considerations

ART	Special Considerations
Tenofovir DF	Renal toxicity, Loss of bone density Improved with TAF instead of TDF TAF approved for eGFR ≥30 mL/min
Abacavir	Must be HLA-B*5701 negative Caution if high initial viral load & in cardiovascular disease
Atazanavir	Avoid PPIs; indirect hyperbilirubinemia, renal & gall stones
Raltegravir	Twice daily administration vs HD not interchangeable Lower barrier to resistance
Ritonavir, Cobi	Drug interactions
Efavirenz	Neuropsychiatric side effects
Rilpivirine	Avoid acid suppressors, must be taken with food Caution if high initial viral load

Treatment Considerations

- Single tablet regimens - preferred
  - Biktarvy® BIC/TAF/FTC
  - Triumeq® DTG/ABC/3TC (only if HLA-B*5701 negative)
  - Dovato® DTG/3TC (if viral load <500,000 copies/mL)
- Single tablet regimens - alternative
  - Genvoya® EVG/c/TAF/FTC
  - Stribild® EVG/c/TDF/FTC
  - Delstrigo™ DOR/TDF/3TC
  - Odefsey® RPV/TAF/FTC
  - Complera® RPV/TDF/FTC
  - Atripla® EFV/TDF/FTC or Symfi® EFV/TDF/3TC
  - Symtuza® DRV/c/TAF/FTC

Lab monitoring throughout therapy

- HIV viral load 2-4 weeks after starting ART no later than 8 weeks (AIII), repeat at 4- to 8- week until undetectable (BIII)
  - Goal is undetectable within 8-24 weeks
  - Then every 3-4 months (AIII)
  - Every 6 months if undetectable after 2 years (AIII)
  - When regimen is modified for toxicity or simplification, repeat viral load within 4 to 8 weeks after change (AIII)
- CD4 count
  - Adequate response to therapy is an increase by 50-150 cells/mm^3 during 1st year of ART
  - 3 months after initiation of ART (AIII), in the 1st 2 years after ART initiation q 3-6 months (BII)
  - If stable CD4 (300-500 cells/mm^3) after 2 years, measure every year (BII)
  - If CD4 >500 cells/mm^3 after 2 years then monitoring optional (CIII)

References

- www.cdc.gov/hiv
- Present case on ECHO http://echo.unm.edu
- Clinical Consultation Center HIV line (800-933-3413)
- AETC National Coordinating Resource Center's *National HIV Curriculum* https://aidsetc.org/nhc
- *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults & Adolescents*. DHHS 12/2019. http://aidsinfo.nih.gov/contentfiles/adultandadolescentgl.pdf
- *Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2018 Recommendations of the International Antiviral Society-USA Panel*. JAMA 2018;320(4):379-396. https://www.iasusa.org/guidelines