Updates to the HHS Adult and Adolescent HIV Treatment Guidelines

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HHS Adult and Adolescent HIV Treatment Guidelines
Updated June 3rd, 2021

- Updated sections:
  - What to start
  - Virologic failure
  - Poor CD4 recovery and persistent inflammation
  - Optimizing ART in the setting of viral suppression
  - Adolescents and young adults with HIV
  - Cisgender women with HIV
  - Substance use disorder
  - TB-HIV coinfection
  - Cost considerations & drug-drug interaction tables

What to Start
Recommended Initial ART Options

HHS (June 2021)[1*] Recommended for Most PWH	IAS-USA (October 2020)[2] Recommended for Most PWH
BIC/FTC/TAF	BIC/FTC/TAF
DTG/ABC/3TC (if B*5701 neg and no HBV) DTG + FTC/TAF or FTC/TDF	DTG + FTC/TAF or FTC/TDF
DTG/3TC (only if VL <500k, no HBV, have baseline genotype results)	DTG/3TC (only if VL <500k, no HBV, no active OI, not rapid start, can closely monitor adherence and VL response, possibly only if CD4 >200)

**Change: moved RAL + 2 NRTI's to recommended in certain clinical situations*

Abbreviations:
BIC – bictegravir, DTG – dolutegravir, ABC – abacavir, 3TC – lamivudine, FTC – emtricitabine
TDF – tenofovir disoproxil fumarate, TAF – tenofovir alafenamide
HBV - hepatitis B virus, PWH – persons with HIV

Sources:
1. HHS: clinicalinfo.hiv.gov 2. IAS-USA: ias-usa.org

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What to Start
HHS June 2021 Update

- Why move raltegravir (RAL) to recommended in certain clinical situations?
  - Updated Tsepamo data show a lower prevalence of neural tube defects associated with DTG use during conception, which means DTG can be prescribed to PWH of childbearing potential & choosing RAL over DTG is no longer necessary
  - RAL has a lower barrier to resistance than DTG and BIC
  - RAL regimens have higher pill burden than other options

Virologic Failure
HHS June 2021 Update

- For patients with virologic failure, changed “A new regimen should include at least two, and preferably three, fully active agents (AI)” to “A new regimen can include two fully active drugs if at least one with a high resistance barrier is included (e.g., DTG or boosted darunavir) (AI)”
  - Why? Accumulating clinical trial data showing that a regimen with two fully active ARV’s effectively achieves viral suppression, provided one drug has high barrier to resistance
- Clinical trial data on use of fostemsavir for patients with multidrug-resistant HIV added

Virologic Failure
2 Drugs Sufficient if 1 Has High Resistance Barrier

- Examples:
  - M184V/I: BIC/FTC/TAF or DTG + FTC/TAF or FTC/TDF
  - Extensive NRTI + NNRTI resistance: DTG + DRV/cobi
  - Extensive NRTI, NNRTI, PI & INSTI resistance: IBA + FTR + OBR

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Virologic Failure
Translating Guidelines to a Practical Strategy

	Low or UD viral load	High viral load
DTG, BIC, or DRV fully active	DTG, BIC, or DRV + ≥1 active ARV	DTG, BIC, or DRV + ≥2 active ARV's until suppressed
No fully active, high resistance barrier option	≥2 active ARV's	≥3 active ARV's

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Fostemsavir (FTR, *Rukobia*)
Brief Review

- **Indication**:
  - Heavily treatment-experienced adults with multidrug resistant HIV-1 failing their current antiretroviral regimen
- **Dosing**:
  - 600 mg orally twice daily, with or without food
- **Drug-drug interactions**
  - Avoid strong cytochrome P450 (CYP) 3A inducers (eg. rifamycins)
  - FTR increases levels of statins, grazoprevir/voxilaprevir, ethinyl estradiol
- **Use During Pregnancy**
  - Insufficient data
- **Common Adverse Events (≥5%)**
  - Nausea (10%)

Source: *Rukobia* Prescribing Information

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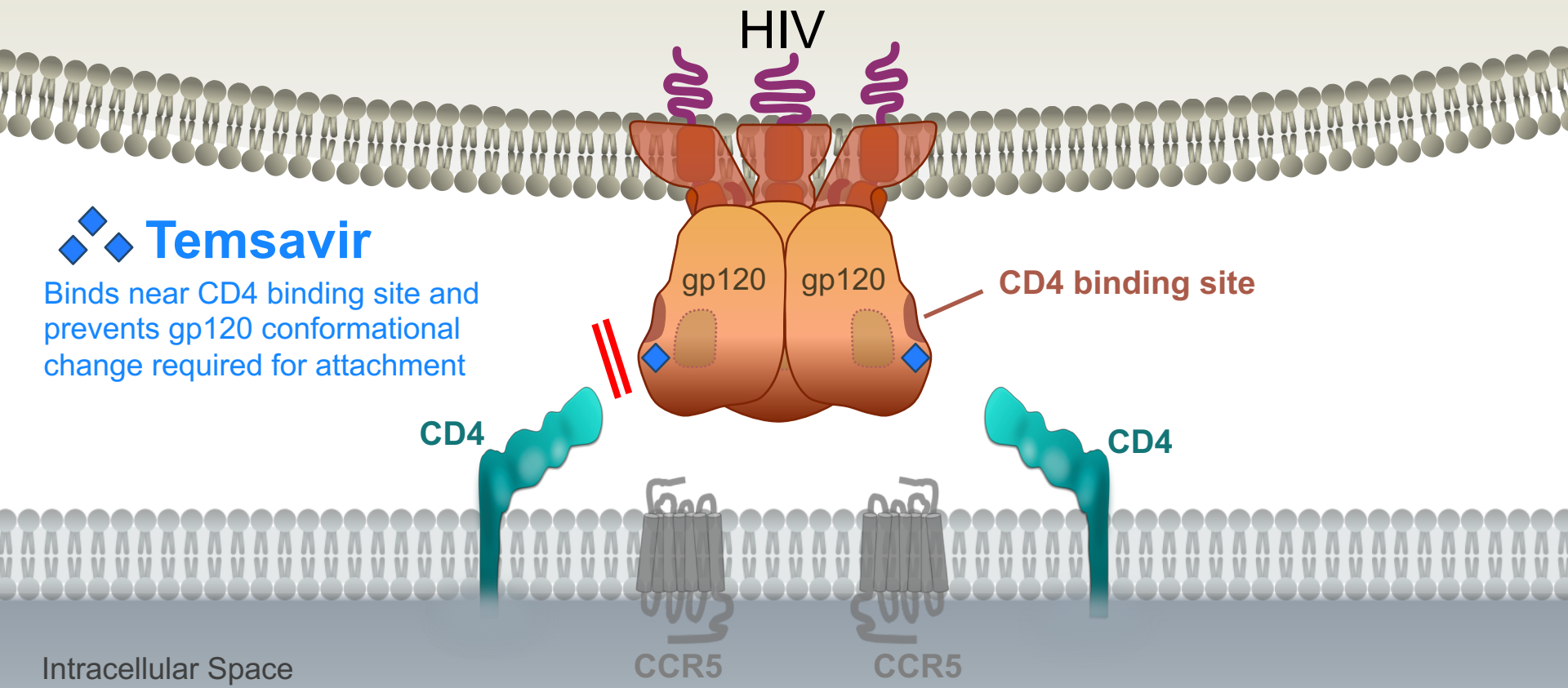
HIV Entry Inhibitors: Attachment Inhibitors
Fostemsavir—prodrug converted to Temsavir

HIV



Poor CD4 Recovery and Persistent Inflammation
HHS June 2021 Update

- Persistently low CD4 counts and immune activation are each associated with increased AIDS- and non-AIDS-related morbidity and mortality, even with viral suppression
- However, there are no proven strategies to improve CD4 cell recovery or reduce immune activation for individuals with ART-mediated viral suppression. **Not recommended**:
  - Adding ARV drugs (ART intensification)
  - Switching ARV drug classes
  - Administration of interleukin-2 (IL-2)

Poor CD4 Recovery and Persistent Inflammation
HHS June 2021 Update

- Efforts to decrease morbidity and mortality during ART-mediated viral suppression should focus on addressing **modifiable risk factors** for chronic disease (e.g., smoking cessation, diet, exercise; treating HTN, HLD)
- In rare cases, CD4 cell counts decline despite suppressive ART in the absence of an obvious clinical cause; severe derangements in interleukin (IL)-7-mediated naive T cell homeostasis have been reported, although the pathophysiology is likely multifactorial

Optimizing ART in the Setting of Viral Suppression
HHS June 2021 Update

- The update to this section primarily focuses on the role of the new long-acting injectable (LAI) intramuscular cabotegravir (CAB) plus rilpivirine (RPV) regimen
- The section describes clinical trial data to date on LAI CAB plus RPV, practical considerations when using these agents, and management of missed doses

Adolescents and Young Adults with HIV
HHS June 2021 Update

- This section was revised extensively to include current epidemiologic data on HIV in adolescents and young adults (AYA) in the US, unique challenges faced by this population compared to their adult counterparts, importance of assisting AYA in navigating optimal transition from pediatric to adult clinical care setting, and strategies to assist AYA in overcoming barriers to adherence

Cisgender Women with HIV
HHS June 2021 Update

- Section updated to include a review of the literature on weight gain in women after ART initiation or switch:
  - Clinicians should consider the possibility of weight gain in women when initiating or changing ART, because women in general and Black women in particular experience greater weight gain with ART as compared to men
  - Underlying mechanisms and impact on CV disease, DM, pregnancy outcomes, and age-related comorbidities unknown
  - Unclear whether switching to a non-INSTI-based regimen results in reversal of weight gain
  - Significant uncertainty whether INSTIs are causing weight gain vs comparator drugs are suppressing weight gain

Cisgender Women with HIV
HHS June 2021 Update

- Updated data from the Botswana Tsepamo study also have been added, describing the prevalence of neural tube defects in infants born to women who were receiving either DTG or efavirenz during conception
- Information regarding hormonal therapy and ARV drug interactions has been updated
- A new subsection offering considerations regarding menopause in women with HIV

Substance Use Disorder
HHS June 2021 Update

- A subsection added discussing factors to consider when contemplating the use of LAI CAB plus RPV in people with substance use disorder (SUD) and HIV
  - Clinical trial data for this regimen were based on participants who have demonstrated medication adherence and viral suppression prior to switching to LAI; knowledge gaps exist regarding the use of LAI in persons with SUD and HIV, especially for those with history of non-adherence

TB-HIV Coinfection
HHS June 2021 Update

- Key update to this section includes recommendations for ARV regimens that can be used if 3-months weekly isoniazid and rifapentine is prescribed for latent TB
- DTG 50 mg once daily may be used with once-weekly rifapentine, provided the patient does not require twice-daily DTG dosing (meaning no confirmed or suspected DTG resistance)

TB-HIV Coinfection
HHS June 2021 Update

- Daily isoniazid for 6 or 9 months: any ARV regimen **(AIII)**
- Once-weekly isoniazid plus rifapentine for 3 months:
  - Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily (in combination with either ABC/3TC or TDF/FTC) **(AII)**
  - Dolutegravir (DTG) 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII)**
- Once-daily isoniazid and rifapentine for 1 month:
  - EFV 600 mg once daily (in combination with either ABC/3TC or TDF/FTC) can be used without dose adjustment **(AI)**
- Rifampin for 4 months also may be considered but clinicians should pay careful attention to potential drug-drug interactions

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