HIV Guideline Updates: Antiretroviral Therapy

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Objectives

Review recent updates in the Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV (HHS)

- What to Start
- Virologic Failure
- Coinfections
  - Latent Tuberculosis (LTBI)
  - Hepatitis B

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What to Start: Initial Combination Antiretroviral Regimens for People with HIV

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What to Start

Abacavir/lamivudine/dolutegravir (DTG/ABC/3TC, Triumeq) **changed to Other Initial Antiretroviral Regimens for Certain Clinical Scenarios** from Recommended Initial Regimens for Most People with HIV.

Why?

- Need for HLA-B*5701 testing
- Potential increase in the risk of cardiovascular events
- Availability of other options for initial therapy

What to Start

No longer recommended as initial therapy:

- Elvitegravir/cobicistat and raltegravir-based regimens
- Boosted atazanavir-based regimens
- Efavirenz-based regimens
- Rilpivirine (RPV)/tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) regimens

Why?

- Higher pill burdens
- More adverse events
- Lower barrier to resistance

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What to Start: Recommended Initial Regimens for Most People with HIV

No History of Taking Injectable Cabotegravir for HIV PrEP	
INSTI + 2NRTIs	**Abbreviation**
Bictegravir-tenofovir alafenamide-emtricitabine	BIC-TAF-FTC
Dolutegravir + Tenofovir alafenamide-emtricitabine	DTG + TAF-FTC
Dolutegravir + [Tenofovir DF-emtricitabine *or* Tenofovir DF-lamivudine]	DTG + [TDF-FTC *or* TDF-3TC]
INSTI + 1NRTI	**Abbreviation**
Dolutegravir-lamivudine (except: HIV >500,000 copies/mL, HBV, no genotype)	DTG-3TC

Source: HHS Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. Sept 16, 2024.

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Virologic Failure

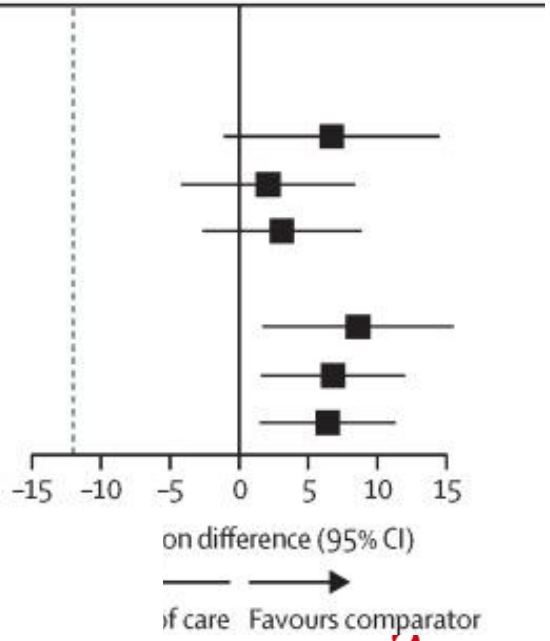
Virologic Failure

Salvage regimens after failure on 2NRTI + NNRTIs now include **dolutegravir + boosted darunavir** (AI Recommendation)

D²EFT

- Evaluation of three second-line ART strategies in PWH failing NNRTI therapy:
  - SOC (DRV/r + 2 NRTI)
  - DTG + DRV/r
  - DTG + TDF/XTC

Viral load at week 48	Standard of care group (ritonavir-boosted darunavir plus two NRTIs), n/N	Comparator group, n/N
Standard of care vs dolutegravir with tenofovir disoproxil fumarate plus either lamivudine or emtricitabine		
<50 c/mL	147/206	227/291
<200 c/mL	174/206	252/291
<400 c/mL	179/206	262/291
Standard of care vs ritonavir-boosted darunavir plus dolutegravir		
<50 c/mL	194/257	222/264
<200 c/mL	222/257	246/264
<400 c/mL	227/257	250/264



Either switch non-inferior in achieving VS; DRV/r + DTG demonstrated statistical superiority

D2EFT Study Group. Lancet HIV 2024.

Virologic Failure

LA CAB/RPV may be used on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART with no resistance to either agent and with shared decision making (CIII Recommendation)

Approach #1: Intensive efforts to achieve VS prior to switch to LA CAB/RPV

Approach #2: Administer LA CAB/RPV in people with viremia unable to achieve viral suppression despite intensive adherence support

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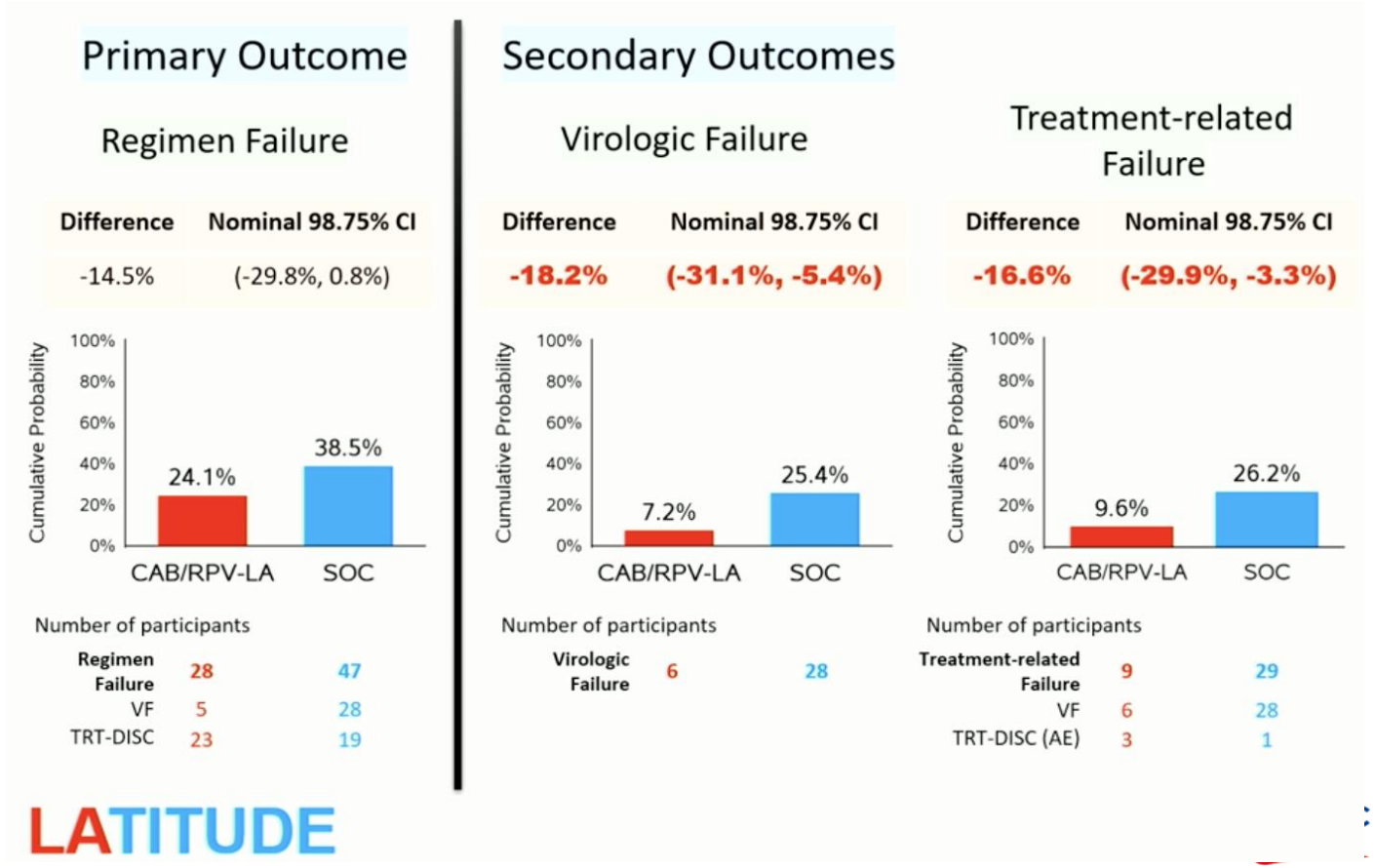
Virologic Failure: LA CAB/RPV

Approach #1: Intensive efforts to achieve VS prior to switch to LA CAB/RPV

- **Why?** LA CAB/RPV studies enrolled participants with VS prior to switch

LATITUDE

- LA ART strategy in people with adherence challenges
- Adherence support, economic incentives to achieve VS on oral ART
- Once suppressed, randomized switch to PO continuation OR monthly LA CAB/RPV
- Based on results, DSMB recommends halting randomization and offering all participants LA CAB/RPV



Rana et al, CROI 2024 Abstract #212

Virologic Failure: LA CAB/RPV

Approach #2: Administer LA CAB/RPV in people with viremia unable to achieve viral suppression despite intensive adherence support

- **Why?** People who can't suppress on orals need another option

- Observational/compassionate use data suggests select people with viremia and poor oral adherence can suppress on CAB/RPV

BUT

- Risk of virologic failure on CAB/RPV associated with risk of new and significant RT and INSTI RAMs
- Recommendation for close monitoring, preference for monthly dosing, novel adherence strategies

Gandhi et al. Ann Intern Med. 2023
Brock et al. Clin Infect Dis. 2024
Mehtani et al. J Acquir Immune Defic Syndr. 2024

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Coinfections

Latent Tuberculosis

For PWH who are VS on a daily DTG based regimen, once daily isoniazid plus rifapentine (1HP) is an acceptable regimen for latent tuberculosis treatment with increase in dosage of DTG to twice daily (AIII).

- 1HP noninferior to 9H in BRIEF-TB, but anchor drug was EFV
- DTG trough concentrations reduced by 50-60% with weekly rifapentine (even so, VS largely maintained in studies of once daily dosing)
- PK study in PWH on daily DTG with dose increase to BID while on 1HP and for 14 days after
  - Trough concentrations comparable to daily dosing DTG without 1HP
  - 97% remained virologically suppressed

Swindells et al. N Engl J Med 2019
Podany et al. Clin Infect Dis. 2024

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Hepatitis B

People with HIV and chronic HBV should be tested for HDV with HDV Ab test followed by HDV RNA if positive.

- Survey of those with HIV/HBV coinfection in US with 4% HDV Ab positivity, of whom 41.7% had detectable RNA
- HBV/HDV coinfection associated with serious liver complications

Ferrante et al. J Viral Hepat 2023.

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Other

Other Updates

- Transplantation in People with HIV (NEW)
- HIV and the Older Person Section
- Substance Use Disorders and HIV
- Transgender People with HIV
- Optimizing Antiretroviral Therapy in the Setting of Viral Suppression
  - Ensure HBV active drugs for those with HBV/HIV coinfection in two drug regimen era
  - More clinical trial data on switch strategies (LA CAB/RPV, extensive drug resistance)

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Take Home Points

- ABC/3TC/DTG is no longer a first choice regimen for ART initiation
- Dolutegravir plus boosted darunavir is now added to potential regimens to use in the setting of virologic failure on 2NRTI + NNRTI regimen
- LA CAB/RPV should be considered for people struggling with oral therapy adherence, with shared decision making
- 1HP for LTBI is an acceptable regimen for PWH currently on daily DTG based regimen
- Screen for HDV in those with HIV/HBV coinfection

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Questions?

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