Advancing HIV Care: New Agents, Personalized Selection, and Prophylactic Strategies

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Objectives

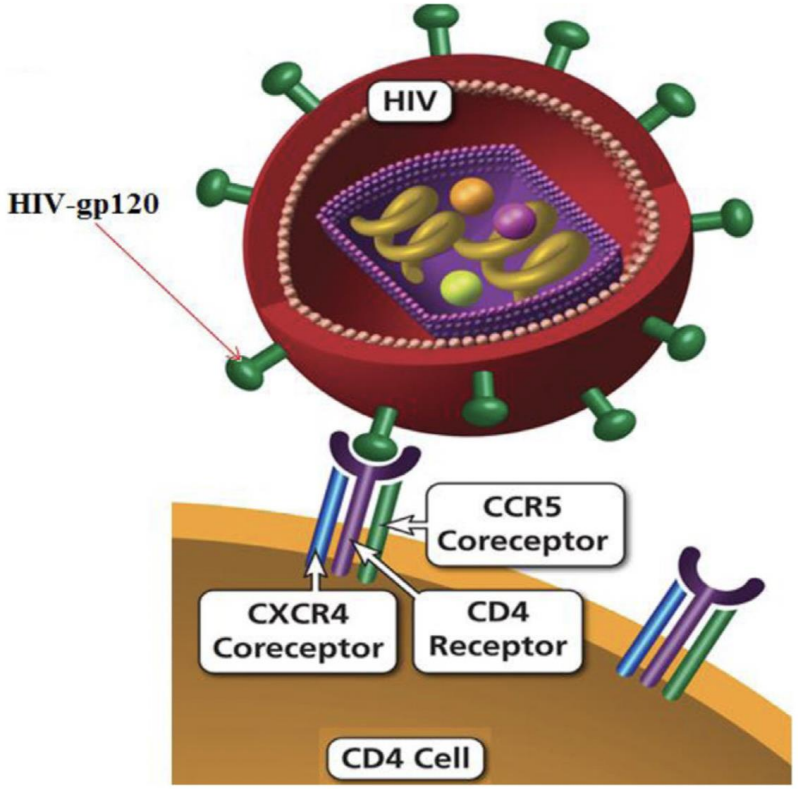
- Recall recent advancements in antiretroviral therapy (ART) and updates to human immunodeficiency virus (HIV) treatment guidelines.
- Identify an appropriate antiretroviral regimen for patients with HIV based on individual patient factors such as co-morbidities, drug resistance, and potential drug interactions.
- Recognize evidence-based monitoring parameters for patients with HIV to effectively adjust opportunistic infection prophylaxis regimens.

Overview

- General Overview of Epidemiology and Treatment
- Recent Advancements in HIV Treatment & Prevention
- ART Regimen Selection: Patient-Specific Considerations
- Opportunistic Infection Prophylaxis
- Summary & Key Takeaways

Background

- HIV is a single-stranded ribonucleic acid (RNA) retrovirus that uses the machinery in host CD4 T-helper cells (T cells) to replicate
  - CD4+ T are critical for coordinating the immune response by interacting with and activating other immune cells, like B cells, macrophages and CD8 T cells
- Once replicated, the viral copies burst through the CD4 cell membrane, destroying the cell in the process
- Billions of T cells are destroyed every day if HIV is not treated adequately



Source: HIV and AIDS. World Health Organization. 2024.
Source: Mokgadi S , Musyoka N, & Onyango M. S. (2019). Theoretical model for the design and preparation of a CNT-ursonic acid drug matrix as HIV-gp120 entry inhibitor. Scientific African.

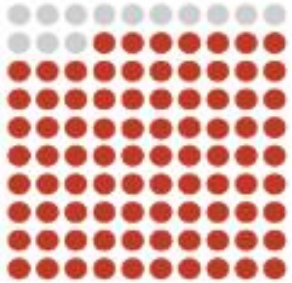
Background

- When HIV continues to replicate, the viral load increases and the CD4 count decreases
- Acquired immunodeficiency syndrome (AIDS) is diagnosed when the CD4 count falls below 200 cells/mm^3 or the patient develops an AIDS-defining condition
  - At this point, the immune system is very weak, making the patient susceptible to AIDS-defining conditions, including but not limited to:
    - Candidiasis of bronchi, trachea, or lungs
    - Kaposi sarcoma
    - Histoplasmosis, disseminated or extrapulmonary

Source: HIV and AIDS. World Health Organization. 2024.

In 2022, an estimated
1.2 million people had HIV.

For every 100 people with HIV



87
knew their
HIV status.

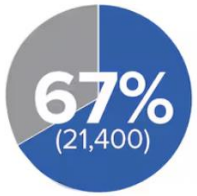
Ending the HIV Epidemic

Overall Goal: Increase the estimated percentage of people with HIV who have received an HIV diagnosis to at least 95% by 2025 and remain at 95% by 2030.

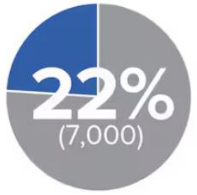
Source: Fast Facts: HIV in the United States. Centers for Disease Control and Prevention. 2024.

Estimated HIV infections in the US by transmission category, 2022

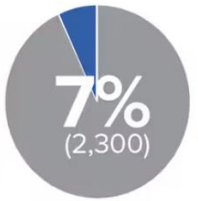
There were **31,800 estimated new HIV infections** in the US in 2022. Of those:



were among gay, bisexual, and other men who reported male-to-male sexual contact*



were among people who reported heterosexual contact



were among people who inject drugs

* Includes infections attributed to male-to-male sexual contact *and* injection drug use (men who reported both risk factors).

Source: CDC. Estimated HIV incidence and prevalence in the United States, 2018–2022. *HIV Surveillance Supplemental Report*, 2024; 29(1).

Ending the HIV Epidemic

Overall Goal: Decrease the estimated number of new HIV infections to 9,300 by 2025 and 3,000 by 2030.

Source: Fast Facts: HIV in the United States. Centers for Disease Control and Prevention. 2024.

Rates of Perinatal HIV Transmission

Perinatal

- Annual perinatal HIV diagnosis rates declined from 1.9 in 2010 to 0.9 in 2019 per 100,000 live births
- Perinatal HIV transmission rates declined from 1.6% in 2010 to 0.9% in 2019

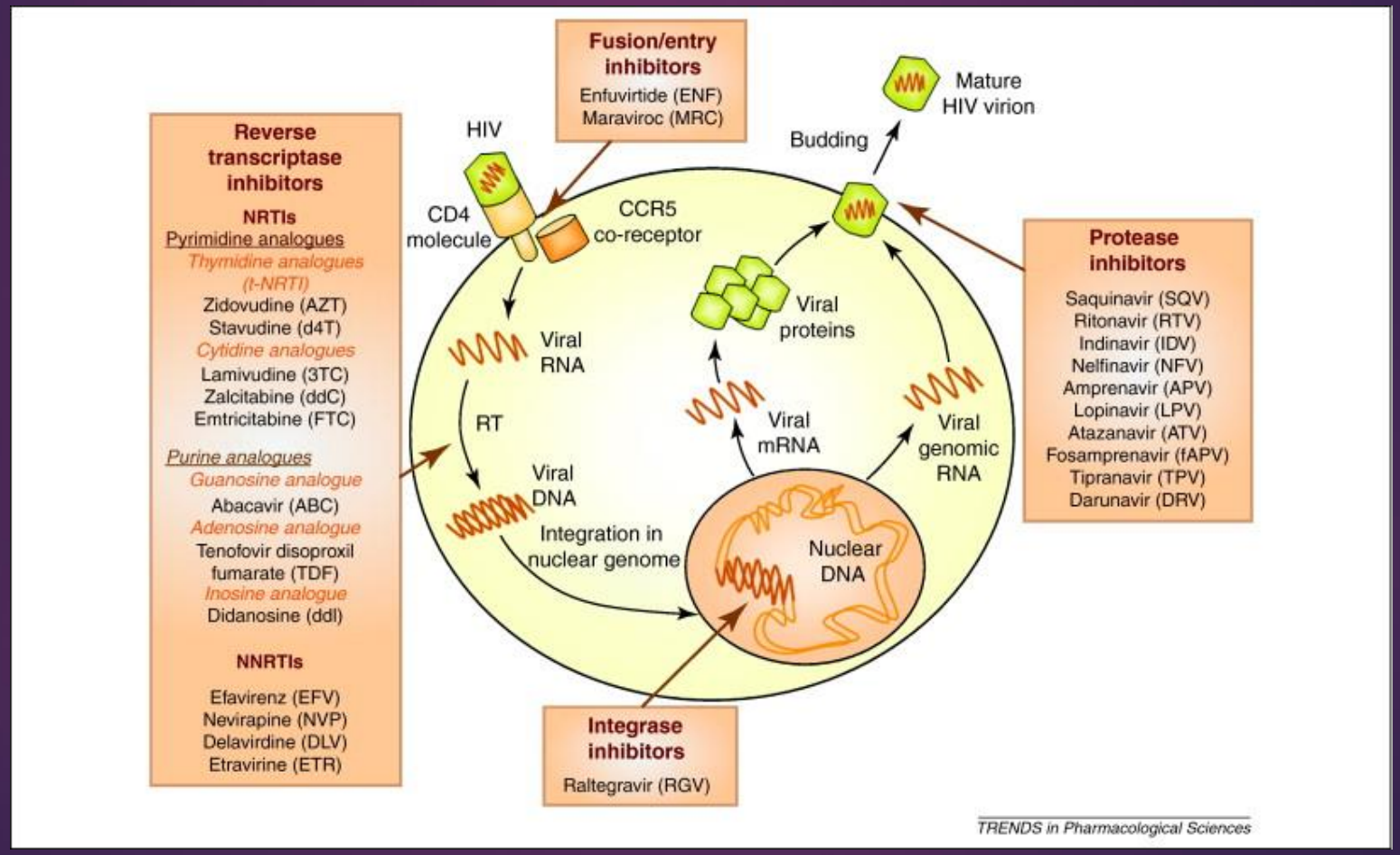
Source: Lampe M, et al. Achieving Elimination of Perinatal HIV in the United States. *Pediatrics*. 2023.

Why is it important?

- In 2022, there were 4,243 HIV-related deaths
- People with HIV who start on effective HIV treatment can live long, healthy lives
- There are many adherence barriers and drug-drug interactions which require active monitoring and patient-centered care
- HIV remains a public health crisis, but with the right tools, providers can help prevent transmission and extend life expectancy

Source: HIV Surveillance Report: Diagnosis, Deaths, and Prevalence of HIV in the United States and 6 Territories and Freely Associated States, 2022.

HIV Treatment Options



Source: Apostolova N, Blas-Garcia A, Esplugues J, et al. Mitochondrial interference by anti-HIV drugs: mechanisms beyond Pol-γ inhibition. Trends in Pharmacological Sciences, 2011.

Recent Advancements in ART and PrEP

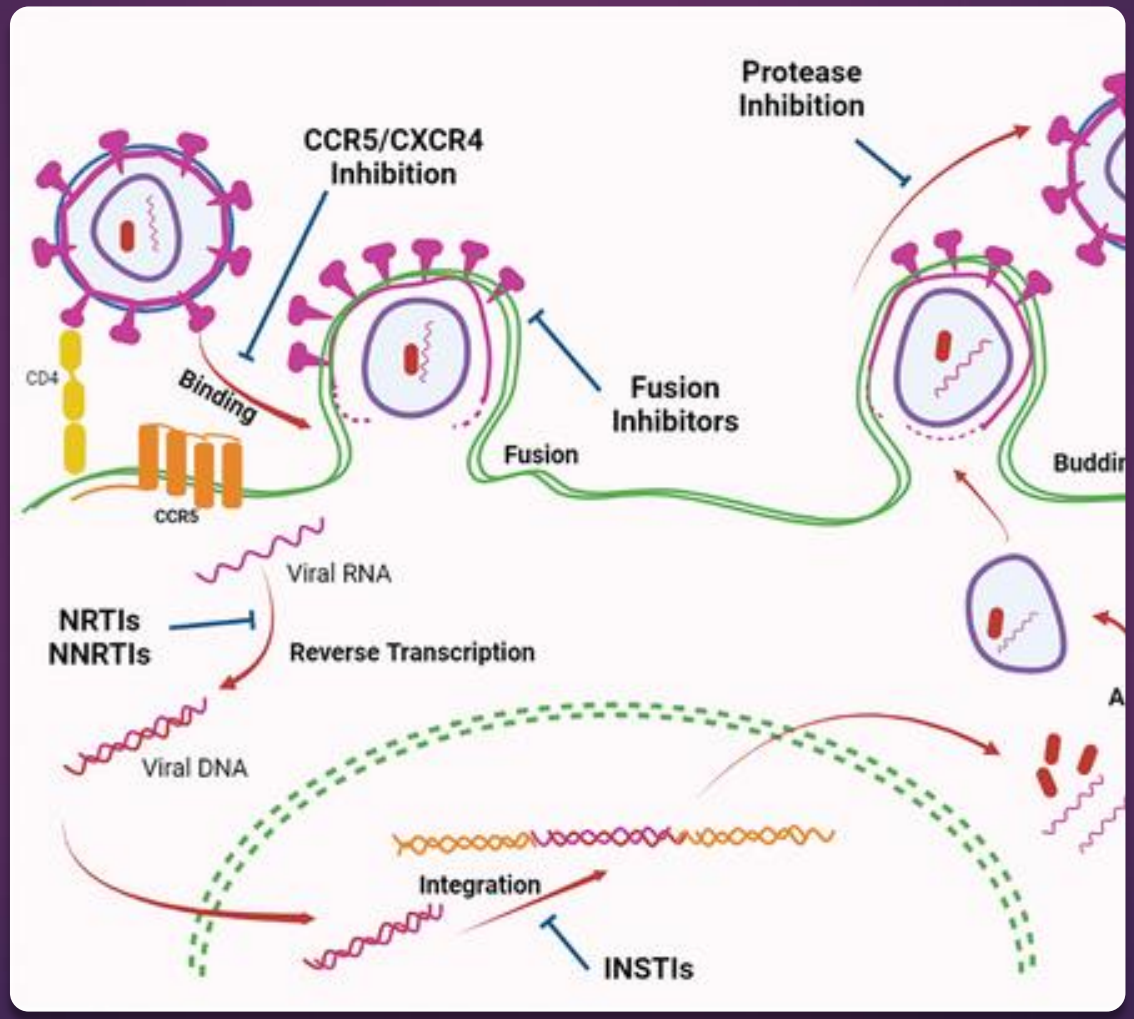
Long-acting injectable Pre-Exposure Prophylaxis (PrEP): cabotegravir

Long-acting injectable ART options (e.g., cabotegravir/rilpivirine [Cabenuva®])

Approval of lenacapavir (Sunlenca®)

Updates to U.S Department of Health and Human Services Panel (DHHS) HIV Guidelines

Cabotegravir (Apretude®)



Source: Taki E, at al. (2022). Cabotegravir/Rilpivirine: the last FDA-approved drug to treat HIV. *Expert Review of Anti-Infective Therapy*.

Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women

Authors: Raphael J. Landovitz, M.D., Deborah Donnell, Ph.D., Meredith E. Clement, M.D., Brett Hanscom, Ph.D., Leslie Cottle, B.A., Lara Coelho, M.D., Robinson Cabello, M.D., +58 , for the HPTN 083 Study Team* Author Info & Affiliations

- 2021 non-inferiority trial
- N = 4566 participants
- Treatment: Long-acting cabotegravir intramuscularly every 8 weeks versus daily oral tenofovir disoproxil fumarate/emtricitabine
- Outcome Measure: Incident HIV infection
- Results:
  - 13 infections in cabotegravir group (0.41/100 person-years)
  - 39 infections in TDF–FTC group (1.22/100 person-years)
  - Hazard ratio: 0.34 (95% CI: 0.18–0.62)
- Conclusion: Cabotegravir was superior to daily oral tenofovir disoproxil fumarate/emtricitabine in preventing HIV infection among cisgender men who have sex with men and at-risk transgender women who have sex with men

Source: Landovitz R. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. 2021. N Engl J Med.

Cabotegravir (Apretude®)

- Dosing Overview:
  - Oral lead-in phase (optional): 30 mg cabotegravir PO daily x 28 days
  - Injection phase (PrEP): two initial IM injections 1 month apart, then every 2 months
- Side effects: injection site reactions, fever, fatigue, diarrhea, nausea, hepatoxicity
- Monitoring parameters: HIV RNA levels, hypersensitivity symptoms, adherence to injection schedule

Source: Apretude (cabotegravir) [prescribing information]. ViiV Healthcare
Source: Centers for Disease Control and Prevention (CDC), US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 update: a clinical practice guideline.

Cabotegravir (Apretude®)

Drug /Class	Interaction	Recommendation
Carbamazepine	↓ cabotegravir plasma concentrations	Risk X: Avoid Combination
Oxcarbazepine		
Phenobarbital		
Phenytoin		
Rifampin		
Rifapentine		

Source: Apretude (cabotegravir) [prescribing information]. ViiV Healthcare
Source: Centers for Disease Control and Prevention (CDC), US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 update: a clinical practice guideline.

Cabotegravir (Apretude®)

- Planned missed injections:
  - If a patient plans to miss a schedule injection by > 7 days, start oral cabotegravir 30 mg daily for up to 2 months
  - Start oral therapy ~ 2 months after the last injection
  - Restart injections on the last day of oral dosing or within 3 days after
  - If oral therapy goes beyond 2 months, switch to a different oral PrEP regimen

Source: Apretude (cabotegravir) [prescribing information]. ViiV Healthcare.

Cabotegravir (Apretude®)

- Second injection missed:
  - ≤ 2 months since first injection: Give ASAP, then continue to follow every 2-month injection dosing schedule
  - > 2 months since first injection: Restart with 600 mg IM, followed by a second 600 mg IM dose 1 month later. Then, continue to follow every 2-month injection dosing schedule

Source: Apretude (cabotegravir) [prescribing information]. ViiV Healthcare.

Cabotegravir (Apretude®)

- Third injection missed:
  - ≤ 3 months since first injection: Give ASAP, then continue to follow every 2-month injection dosing schedule
  - > 3 months since first injection: Restart with 600 mg IM, followed by a second 600 mg IM dose 1 month later. Then, continue to follow every 2-month injection dosing schedule

Source: Apretude (cabotegravir) [prescribing information]. ViiV Healthcare.

Cabotegravir and rilpivirine (Cabenuva®)

- Mechanism Of Action:
  - Cabotegravir: An integrase strand transfer inhibitors (INSTI) that blocks the HIV integrase, preventing the insertion of viral DNA into the host cell's genome
  - Rilpivirine: A non-nucleoside reverse transcriptase inhibitor (NNRTI) that inhibits the reverse transcriptase enzyme, stopping the conversion of viral RNA into DNA and halting replication early

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024.
Image from Business Wire.

Cabotegravir and rilpivirine (Cabenuva®)

- Cabotegravir + rilpivirine intramuscular (IM)
- Indication: HIV infection treatment in virologically suppressed (viral load < 200) patients with no resistance to either drug
- Monitoring parameters: Liver function tests (LFTs), injection-related reactions, signs and symptoms of hypersensitivity
- Dosing:
  - Optional oral lead-in: cabotegravir + rilpivirine PO x ~ 28 days
  - IM injection every 4 weeks or every 8 weeks
- Ideal patients:
  - Struggling with daily adherence
  - Stable clinic access

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024.

Cabotegravir and rilpivirine (Cabenuva®)

- Planned missed injections:
  - Monthly injection dosing: It a patient plans to miss a scheduled injection visit by > 7 days, administer oral therapy for up to 2 months
  - The first dose of oral therapy should be administered 1 month (+/- 7 days) after the last injection and continued until the day the injection dosing is restarted

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024.

Cabotegravir and rilpivirine (Cabenuva®)

- Unplanned missed injections:
  - Monthly dosing:
    - ≤ 2 months since last injection: continue with cabotegravir 400 mg and rilpivirine 600 mg IM monthly injections
    - > 2 months since last injection: reinitiate with cabotegravir 600 mg and rilpivirine 900 mg IM injections, then continue to follow the cabotegravir 400 mg and rilpivirine 600 mg IM monthly injections

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024.

Cabotegravir and rilpivirine (Cabenuva®)

- Unplanned missed injections:
  - Every-2-month dosing: Second injection missed
    - ≤ 2 months since first injection: administer cabotegravur 600 mg and rilpivirine 900 mg IM injections as soon as possible, then continue to follow the every-2-month injection dosing schedule
    - > 2 months since first injection: reinitiate with cabotegravir 600 mg and rilpivirine 900 mg IM once, followed by cabotegravir 600 mg and rilpivirine 900 mg IM 1 month later. Then, continue to follow the every-2-month injection dosing schedule

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024.

Cabotegravir and rilpivirine (Cabenuva®)

- Unplanned missed injections:
  - Every-2-month dosing: Third or subsequent injections missed
    - ≤ 3 months since last injection: administer cabotegravur 600 mg and rilpivirine 900 mg IM injections as soon as possible, then continue to follow the every-2-month injection dosing schedule
    - > 3 months since last injection: reinitiate with cabotegravir 600 mg and rilpivirine 900 mg IM once, followed by cabotegravir 600 mg and rilpivirine 900 mg IM 1 month later. Then, continue to follow the every-2-month injection dosing schedule

Cabotegravir and rilpivirine (Cabenuva®)

Drug /Class	Interaction	Recommendation
Carbamazepine	↓ cabotegravir & rilpivirine plasma concentrations	Risk X: Avoid Combination
Oxcarbazepine		
Phenobarbital		
Phenytoin		
Rifampin		
Rifapentine		
St John's Wort	↓ rilpivirine levels	
Dexamethasone	↓ rilpivirine levels	

Source: Cabenuva (cabotegravir and rilpivirine) [prescribing information]. ViiV Healthcare. September 2024

Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial

Cissy Kityo, PhD [a] · Ivan K Mambule, MBChB [a] · Joseph Musaazi, MSc [b] · Simiso Sokhela, MBChB [c] · Henry Mugerwa, MSc [a] · Gilbert Ategeka, MBChB [d] · et al. Show more

- 2022 non-inferiority trial
- Study Population: 512 participants with HIV RNA < 50 copies/mL on stable oral antiretroviral with no history of virologic failure
- Treatment Arms: Intramuscular cabotegravir (600 mg) + riplivirine (900 mg) every 8 weeks versus continued daily oral antiretroviral therapy
- Outcome Measure: Week 48 viral load below 50 copies per mL
- Results:
  - 96% on long-acting therapy-maintained suppression
  - 97% on oral therapy-maintained suppression
  - Difference: –0.8% (95% CI: –3.7 to 2.3) → met criteria for non-inferiority
- Conclusion: long-acting therapy were non-inferior to oral antiretroviral and well-tolerated

Source: Kityo, C. Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial. The Lancet.

Lenacapavir (Sunlenca®)

Mechanism Of Action:

- First-in-class capsid inhibitor targeting the HIV-capsid protein
- Blocks multiple stages of the viral cycle: nuclear import, viral assembly, capsid disassembly

Resistance

- No cross-resistance with other ART classes – ideal for multidrug-resistant HIV-1

Source: Sunlenca (lenacapavir) [prescribing information]. Foster City, CA: Gilead Sciences Inc; November 2024.

Lenacapavir (Sunlenca®)

- Indication: Heavily treatment-experienced adults with multidrug-resistant HIV
- Dosing:
  - Oral lead-in (optional): 600 mg PO x 2 days, then 300 mg PO day 8
  - Maintenance: 927 mg SC every 6 months
- Monitoring: signs/symptoms of injection-site reactions
- Use with optimized background regimen (not monotherapy)
- Not yet approved for PrEP, but, currently under investigation

Source: Sunlenca (lenacapavir) [prescribing information]. Foster City, CA: Gilead Sciences Inc; November 2024.

Lenacapavir (Sunlenca®)

- Planned missed injections:
  - If a patient plans to miss a scheduled 6-month injection visit by > 2 weeks during the maintenance period, lenacapavir 300 mg orally once every 7 days may be taken for up to 6 months before injections resume
  - Resume maintenance injection dosage within 7 days after last oral dose
- Unplanned missed injections:
  - If > 28 weeks elapse since last injection during the maintenance period and oral tablets have not been taken, restart initiation dose from day 1

Source: Sunlenca (lenacapavir) [prescribing information]. Foster City, CA: Gilead Sciences Inc; November 2024.

Lenacapavir (Sunlenca®)

Drug /Class	Interaction	Recommendation
Carbamazepine	↓ lenacapavir plasma concentrations	Risk X: Avoid Combination
Oxcarbazepine		
Phenobarbital		
Phenytoin		
Rifampin		
Rifapentine		

Source: Sunlenca (lenacapavir) [prescribing information]. Foster City, CA: Gilead Sciences Inc; November 2024.

Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection

Authors: Sorana Segal-Maurer, M.D., Edwin DeJesus, M.D., Hans-Jurgen Stellbrink, M.D., Antonella Castagna, M.D., Gary J. Richmond, M.D., Gary I. Sinclair, M.D., Krittaecho Siripassorn, M.D., +10 , for the CAPELLA Study Investigators* Author Info & Affiliations

- 2022 randomized, double-blind, placebo-controlled, multicenter study
- N = 72 participants with multidrug-resistant HIV-1
- Intervention: Participants received oral lenacapavir for 14 days, followed by subcutaneous lenacapavir injections every 6 months, in combination with an optimized background regimen
- Primary Endpoint: Reduction of at least 0.5 $\log_{10}$ copies/mL in HIV-1 RNA by day 15
- Results: At day 15, 88% of patients in the lenacapavir group (21 out of 24) experienced a viral load decrease of at least 0.5 $\log_{10}$ copies per mL, compared to 17% in the placebo group (2 out of 12), with an absolute difference of 71 percentage points (95% CI: 35 to 90), demonstrating strong antiviral efficacy.
- This study found that lenacapavir is effective in reducing viral load and achieving viral suppression in patients with multidrug-resistant HIV-1 infection

Source: Segal-Maurer, S, DeJesus, E, Stellbrink, H. J, et al. (2022). Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection. N Engl Jour Med.

Assessment Question 1

What is the recommended dosing schedule for intramuscular cabotegravir when used for HIV pre-exposure prophylaxis (PrEP) after the initial oral lead-in period?

A. Injections every two months
B. Two injections given one month apart, followed by injections every two months
C. An oral dose taken daily for three months, followed by monthly injections
D. One injection every three months without an oral lead-in period

Assessment Question 1: Correct Response

What is the recommended dosing schedule for intramuscular cabotegravir when used for HIV pre-exposure prophylaxis (PrEP) after the initial oral lead-in period?

A. Injections every two months
B. Two injections given one month apart, followed by injections every two months
C. An oral dose taken daily for three months, followed by monthly injections
D. One injection every three months without an oral lead-in period

DDHS 2023-2024 Guideline Updates: First-Line ART for Most People with HIV

INSTI-Based Regimen	**INSTI plus 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**
	Bictegravir/tenofovir alafenamide/emtricitabine
	Dolutegravir plus (tenofovir alafenamide OR tenofovir disoproxil fumarate) plus (emtricitabine or lamivudine)
	INSTI plus 1 NRTI
	Dolutegravir/lamivudine *Avoid if: • Viral load > 500,000 copies/mL • HBV status unknown

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

DDHS 2023-2024 Guideline Updates

- Initial ART Regimens
  - Dolutegravir/abacavir/lamivudine moved from "Recommended for Most" to "Certain Clinical Scenarios" due to:
    - Need for HLA-B*5701 testing
    - Possible increased cardiovascular risk

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

DDHS 2023-2024 Guideline Updates

- No longer recommended as initial therapy due to pill burden, side effects, or lower resistance barrier:
  - Elvitegravir/cobicistat
  - Raltegravir
  - Boosted atazanavir
  - Efavirenz
  - Rilpivirine with tenofovir disoproxil fumarate and emtricitabine

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

DDHS 2023-2024 Guideline Updates to Virologic Failure

- For those who fail NNRTI + 2 NRTIs, dolutegravir + boosted darunavir is recommended
- For those who cannot reach or maintain viral suppression on oral ART despite intensive adherence, the Panel recommends the use of long-acting injectable cabotegravir and rilpivirine (LA CAB/RPV)

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Hepatitis B Virus/HIV Coinfection

- Because ~4% of people with HBV/HIV coinfection are also found to have hepatitis D virus (HDV), experts now recommend screening for HDV in people with HBV/HIV coinfection
- Screen for HBV before switching to NRTI-sparing or NRTI-limiting regimens in people who are not known to have HBV infection
  - The Panel also recommends HBV vaccination for those found to be nonimmune to HBV
- The Panel no longer recommends pegylated interferon for HBV in HIV

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Individualization and ART

- Renal/hepatic function
- HLA-B*5701 status
- Comorbidities (e.g., diabetes, CVD, CKD)
- Drug-drug interactions
- Resistance mutations
- Adherence barriers (pill burden, access, lifestyle)

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Overview of Preferred Initial Regimens

- INSTI-based regimens are first-line unless contraindicated:
  - Bictegravir/tenofovir alafenamide/emtricitabine (Biktarvy®)
  - Dolutegravir + tenofovir alafenamide/emtricitabine (Descovy®) or tenofovir disoproxil/emtricitabine (Truvada®)
  - Dolutegravir/lamivudine (Dovato®)
- Avoid two-drug regimens if:
  - Viral load > 500,000 copies/mL
  - HBV status unknown
    - If HBV/HIV coinfection is present, another HBV-active drug should be added

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Renal Dysfunction & ART

- Tenofovir disoproxil → caution if eGFR < 60 mL/min/1.73m^2 → risk of nephrotoxicity & bone loss
- Tenofovir alafenamide (TAF) preferred in CKD (can use if eGFR > 30)
- Abacavir → safe in renal dysfunction
- Adjust lamivudine, emtricitabine if eGFR < 50 mL/min/1.73m^2

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Cardiovascular Disease, Metabolic Concerns

- Abacavir: Increased myocardial infarction risk in patients with pre-existing cardiovascular disease
- Protease inhibitors (PIs) (e.g. atazanavir, darunavir, lopinavir) + ritonavir/cobicistat: can raise lipids, glucose
- INSTIs: neutral to slightly increased weight gain (especially in women, Black patients)
- Prefer unboosted INSTIs + TAF or TDF in CVD

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

The Role of Pharmacogenomics: HLA-B*5701

- Screen all patients before starting abacavir
- Positive = contraindication → increased risk of fatal hypersensitivity
- If negative: abacavir can be used if no other contraindication

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

HBV Coinfection Considerations

- Treat both HIV and HBV simultaneously
- Use tenofovir (TDF or TAF) + emtricitabine or lamivudine
- Avoid lamivudine or emtricitabine monotherapy for HBV --> resistance
- If unable to use tenofovir: add entecavir to HIV regimen

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Drug-Drug Interactions

- Watch for:
  - Acid reducers + rilpivirine → decreased absorption
    - Acid reducers raise gastric pH, reducing rilpivirine solubility and thus absorption
  - Statins + boosted PIs → increased myopathy risk
    - PIs cause CYP3A4 inhibition → increases statin levels
  - Anticonvulsants (carbamazepine, phenytoin) → decreased ART levels
    - Anticonvulsants cause CYP3A4 induction → increased metabolism of many antiretrovirals
  - Metformin + dolutegravir → increased metformin exposure
    - Dolutegravir inhibitors renal organic cation transporter 2 (OCT2) → reduces metformin clearance

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Assessment Question 2

DW is a 44 year-old male with HIV, diabetes, neuropathy and chronic kidney disease. CD4 count is 151 cells/mm3, viral load 70,600 copies/mL, serum creatinine 2.34 mg/dL, and HLA-B *5701 negative. Which of these following regimens is listed as "preferred" by current guidelines as an initial regimen.

A. Raltegravir + abacavir + lamivudine daily
B. Darunavir + ritonavir + emtricitabine/tenofovir disoproxil fumarate daily
C. Bictegravir, emtricitabine, and tenofovir alafenamide daily
D. Dolutegravir + lamivudine daily

Assessment Question 2: Correct Response

DW is a 44 year-old male with HIV, diabetes, neuropathy and chronic kidney disease. CD4 count is 151 cells/mm3, viral load 70,600 copies/mL, serum creatinine 2.34 mg/dL, and HLA-B *5701 negative. Which of these following regimens is listed as "preferred" by current guidelines as an initial regimen.

A. Raltegravir + abacavir + lamivudine daily
B. Darunavir + ritonavir + emtricitabine/tenofovir disoproxil fumarate daily
C. Bictegravir, emtricitabine, and tenofovir alafenamide daily
D. Dolutegravir + lamivudine daily

Key Labs in HIV Monitoring

- CD4 Count: Immune status, opportunistic infection risk
  - 500 cells/mm^3 = normal immune function
  - < 200 cells/mm^3 = severe immunosuppression
- HIV Viral Load
  - Goal: undetectable (< 20– 50 copies/mL)
- Others: Comprehensive metabolic panel, complete blood count, lipids, renal/hepatic panels

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services.

Opportunistic Infections

- HIV patients are more susceptible to infections because the virus **targets and destroys CD4+ T cells**, which are essential for immune function
- Infections that occur due to a weakened immune system (CD4 < 200 cells/$mm^{3)}$
- Common in untreated or advanced HIV/AIDS

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Pneumocystis jirovecii (PCP)

- PCP is a potentially life-threatening opportunistic fungal infection that commonly affects immunocompromised individuals

CD4 < 200 cells/mm^3

CD4% < 14%

History of oropharyngeal candidiasis or AIDS-defining illness

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

PCP Prophylaxis Agents

Preferred:

- Sulfamethoxazole/Trimethoprim (SMX/TMP) 800/160 mg PO daily

Alternative Regimens:

- Dapsone 100 mg PO daily
  - Screen for G6PD deficiency before initiation
- Atovaquone 1500 mg PO daily
  - Option for patients with sulfa allergies or renal dysfunction
- Aerosolized Pentamidine 300 mg via nebulizer once monthly
  - Less systemic absorption
  - Does not provide protection against toxoplasmosis

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Clinical Pearls

Drug	Dose Adjusted?	Drug-Drug Interactions
SMX/TMP	Renally dose adjusted if CrCl < 30	Warfarin, phenytoin, oral hypoglycemics
Dapsone	None	Rifampin, trimethoprim, probenecid
Atovaquone	None	Rifampin, rifabutin, PIs
Pentamidine	Renally dose adjusted if CrCl < 10	Fewer interactions due to inhaled route

Toxoplasmosis Prophylaxis

- A parasitic infection caused by *Toxoplasma gondii*
- Can cause severe encephalitis in immunocompromised individuals

CD4 < 100 cells/mm^3

+

Positive for *Toxoplasma gondii* immunoglobulin G

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Toxoplasmosis Prophylaxis Agents

Preferred:

- SMX/TMP 800 mg/160 mg tablet PO daily

Alternative Regimens:

- Dapsone 50 mg daily + (Pyrimethamine 50 mg + Leucovorin 25 mg) PO weekly
- Atovaquone 1,500 mg ± Pyrimethamine 25 mg + Leucovorin 10 mg PO daily

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Clinical Pearls

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Dapsone	None	Rifampin, trimethoprim, probenecid
Atovaquone	None	Rifampin, rifabutin, efavirenz, PIs
Pyrimethamine	None	Zidovudine, sulfonamides, methotrexate, trimethoprim, phenytoin
Leucovorin	None	Fluorouracil, methotrexate, phenytoin, phenobarbital

Mycobacterium avium complex

- A bacterial infection caused by *Mycobacterium avium* and *Mycobacterium intracellulare*
- Can cause disseminated infection (fever, weight loss, anemia, hepatosplenomegaly)

CD4 < 50 cells/mm^3 + Not on fully suppressive ART

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Mycobacterium avium complex Prophylaxis Agents

Preferred:

- Azithromycin 1200 mg PO once weekly

Alternative Regimens:

- Clarithromycin 500 mg PO twice daily
- Azithromycin 600 mg PO twice weekly

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Assessment Question 3

- CW, is a 42 -year-old male who presents for a routine follow-up visit. His most recent CD4 count is 150 cells/mm^3, and his HIV viral load is undetectable. Given his immunocompromised status, you are considering initiating prophylaxis for *Pneumocystis jirovecii* pneumonia. Assuming no contraindications to any options, which of the following is the most appropriate prophylaxis for this patient based on current guidelines?

A. Initiate sulfamethoxazole-trimethoprim (SMX- TMP) 800 mg of sulfamethoxazole and 160 mg of trimethoprim daily
B. Recommend no prophylaxis, as his viral load is suppressed
C. Initiate atovaquone 750 mg daily
D. Initiate dapsone 100 mg daily

Assessment Question 3: Correct Response

- CW, is a 42 -year-old male who presents for a routine follow-up visit. His most recent CD4 count is 150 cells/mm³, and his HIV viral load is undetectable. Given his immunocompromised status, you are considering initiating prophylaxis for *Pneumocystis jirovecii* pneumonia. Assuming no contraindications to any options, which of the following is the most appropriate prophylaxis for this patient based on current guidelines?

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C. Initiate atovaquone 750 mg daily

D. Initiate dapsone 100 mg daily

Opportunistic Infection Prophylaxis

Infection	CD4 Threshold	Prophylaxis	Criteria for Discontinuing
Pneumocystitis jirovecii	< 200 cells/mm^3	SMX/TMP	CD4 count > 200 cells/mm^3 for > 3 months on ART
Toxoplasmosis	< 100 cells/mm^3	SMX/TMP	Can consider when CD4 count is 100-200 cells/mm^3 and viral load has been undetectable for $\geq$ 3 to 6 months
Mycobacterium avium complex (MAC)	< 50 cells/mm^3	Azithromycin	Taking fully suppressive ART

Source: Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America.

Summary & Key Takeaways:

- ART is evolving
- Guideline updates emphasize individualization
- PrEP is expanding
- Monitoring remains essential
- Prophylaxis is CD4-based

Acknowledgements

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THANK YOU!!

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