

CMEO BriefCase

Switching ART Due to Treatment Resistance

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Learning Objective:

Implement ART switching strategies to overcome HIV treatment resistance.

Patient Case: Luis

35 yo male presents with acute HIV:

- Took oral FTC/TDF for PrEP x 6 years but struggled with daily adherence due to frequent travel
- Switched to CAB-LA ~ 4 months ago due to adherence issues
- Took 30-day oral CAB lead-in followed by 2 loading + 1 maintenance dose of CAB-LA, administered last week with HIV test sent out same day



Last Week's Test Results

HIV-1/2 Ag/Ab: reactive
HIV-1/2 Ab: negative
HIV-1 RNA: detected
at 9.2 single copies/mL

Repeat Test Results

HIV-1/2 Ag/Ab: reactive
HIV-1/2 Ab: negative
HIV-1 RNA: detected
at 8.6 single copies/mL

Ab = antibody; Ag = antigen; CAB = cabotegravir; FTC = emtricitabine, LA = long acting; PrEP = pre-exposure prophylaxis;
TDF = tenofovir disoproxil; yo = year old

Audience Response



According to DHHS Guidelines, what next steps are recommended for people with confirmed acute HIV taking CAB-LA for PrEP?

- A. Delay ART initiation until HIV genotype test results return
- B. Delay ART until seroconversion
- C. Initiate ART with INSTI-containing regimen
- D. Initiate ART with boosted DRV/(TAF or TDF)/(FTC or 3TC)
- E. I don't know

Audience Response

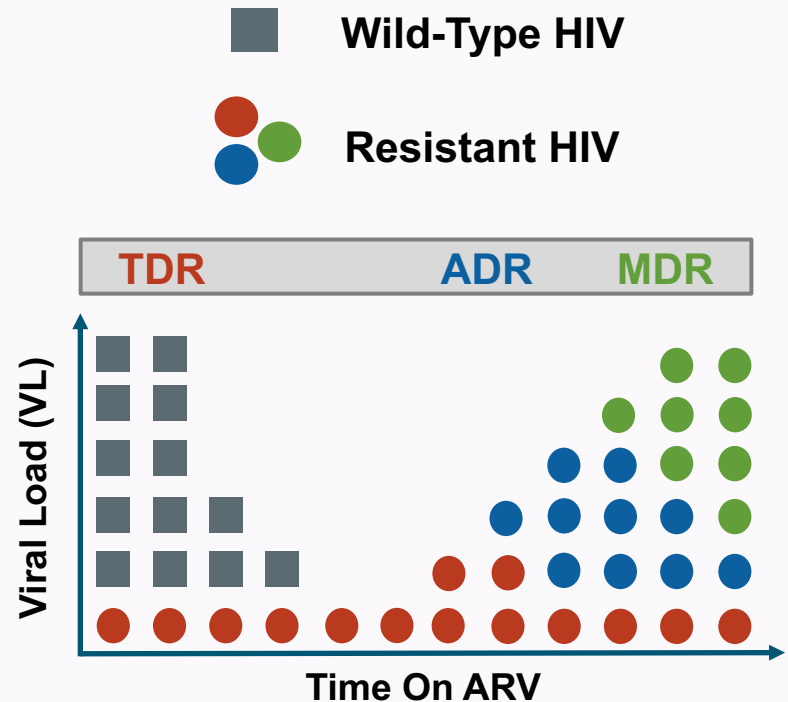


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- D. **Initiate ART with boosted DRV/(TAF or TDF)/(FTC or 3TC)**
- E. I don't know

Etiology of HIV Drug Resistance

- **Acquired Drug Resistance (ADR)** develops when HIV mutations emerge due to viral replication in individuals receiving antiretroviral (ARV) agents.
- **Transmitted Drug Resistance (TDR)** occurs when previously uninfected individuals are infected with ARV resistant HIV.
- **Multi-Drug Resistance (MDR)** occurs when multiple HIV mutations cumulatively resistant to multiple ARV agents and classes are present in the same individual.



Paths to PrEP-Resistant HIV



Breakthrough HIV with PrEP use	Oral PreP (FTC/TDF or FTC/TAF)	Injectable PrEP (CAB-LA)
Suboptimal adherence:	Possible TDR or wild-type	Rare TDR or wild-type
Continued use with undiagnosed HIV:	Rare ADR	Possible ADR (LEVI syndrome)
Common drug-resistant mutations:	K65R and M184I/V	Q148R and N155H
Signs and symptoms:	<ul style="list-style-type: none"> •EXPLOSIVE viral replication <ul style="list-style-type: none"> •Flu-like onset •Seroconversion detectable within 1-2 weeks 	<ul style="list-style-type: none"> •SMOLDERING viral replication <ul style="list-style-type: none"> •Little to no symptoms •Seroconversion delayed many months; assay reversion common

LEVI = long-acting early viral inhibition syndrome

Gibas KM, et al. *Drugs*. 2019;79(6):609-619. Eshleman SH, et al. *J Infect Dis*. 2022;225(10):1741-1749. Rhee SY, et al. *Antiviral Res*. 2022;208:105427.

Audience Response



Which of the following ART regimens is recommended for empiric initiation in people with no prior CAB-LA exposure who become infected with HIV while taking oral PrEP?

- A. BIC/TAF/FTC
- B. DTG/3TC
- C. DTG/ABC/3TC
- D. DOR/TDF/3TC
- E. I don't know

Audience Response



Which of the following ART regimens is recommended for empiric initiation in people with no prior CAB-LA exposure who become infected with HIV while taking oral PrEP?

- A. **BIC/TAF/FTC**
- B. DTG/3TC
- C. DTG/ABC/3TC
- D. DOR/TDF/3TC
- E. I don't know

ART Initiation in PrEP-Breakthrough HIV

- **Rapid ART initiation in confirmed HIV with PrEP exposure:**
 - Draw genotype resistance testing sample prior to first dose, but do not wait for results to initiate empiric ART.
 - Modify ART as needed when resistance test results return.
 - Note HIV RNA < 1000 copies/mL may produce unreliable genotype results; consider proviral assay if available*.
- **If only exposed to oral PrEP, empiric ART options are:**
 - BIC/TAF/FTC
 - DTG/(TDF or TAF)/(3TC or FTC)
 - Boosted DRV/(TDF or TAF)/(3TC or FTC)
- **If ever exposed to CAB-LA for PrEP:**
 - Include integrase in genotype resistance testing.
 - Use boosted DRV/(TDF or TAF)/(3TC or FTC) for empiric ART.

*The usefulness of proviral assays in the clinic is still under investigation and has yet to be fully determined.

U.S. Department of Health and Human Services [DHHS]. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (HIV Treatment Guidelines). Clinical Info HIV.gov Website. 2023. <https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf>.

Patient Case: Luis

Luis was initiated on empiric ART with DRV/COBI/TAF/FTC and returned to discuss his HIV resistance and monitoring test results 3 weeks later.



- Complains new medication is giving him GI side effects (abdominal distention, diarrhea, etc.) which makes him not want to take it, especially with food since he has no appetite.
- Asks if there are any other options that don't need to be taken with food and won't give him the same GI issues, preferably a smaller pill or an injection for easier adherence.
- Genotype resistance testing returned inconclusive.
- HIV monitoring returned viral load < LLOD, absolute CD4 count 524 cells/mm³, and all other labs WNL.

GI = gastrointestinal, COBI = cobicistat; LLOD = lower limit of detection; WNL = within normal limits

Patient Case: Luis

Luis traveled to Mexico to care for his sick mother and became lost to follow-up. He returns over a year later extremely viremic.

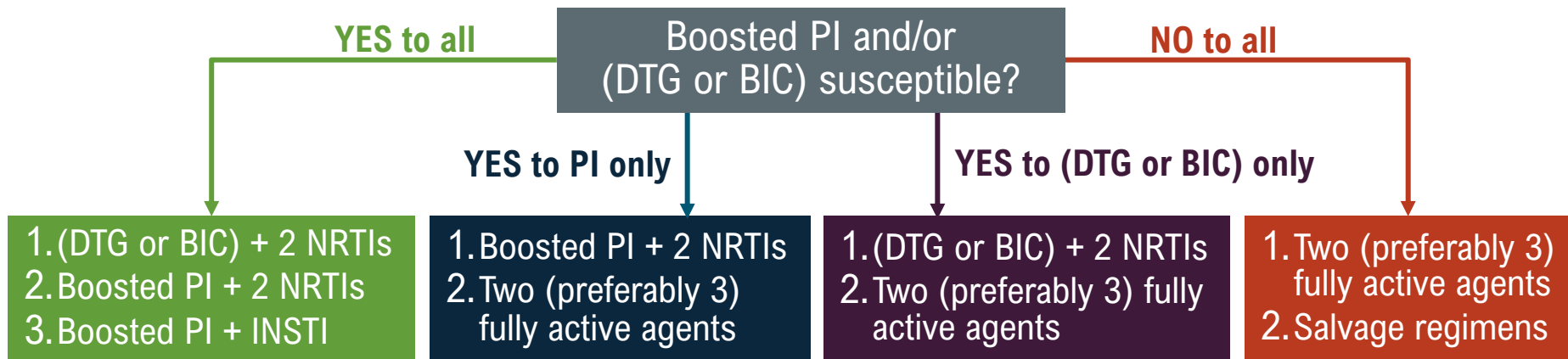


- Due to difficulty accessing HIV specialists and medications in Mexico, Luis cycled on and off several different ARV regimens and has not taken any medications for months.
- HIV RNA is $> 10,000$ copies/mL and CD4 count is 350 cells/mm³.
- HIV genotype resistance testing shows K65R, M184I/V, K103N, and Q148R mutations, indicating Luis now has MDR to NRTIs, NNRTIs, and INSTIs.

NRTI = nucleoside/nucleotide reverse transcriptase inhibitors, NNRTI = Non-nucleoside reverse transcriptase inhibitors

ART Strategies for Viremic MDR HIV

Ideal regimen: ≥ 2 fully active agents from ≥ 2 different classes that can tolerably achieve and maintain viral suppression



Managing MDR HIV is extremely complex.
Always seek expert consultation.

Novel ARVs for MDR HIV:
ibalizumab, fostemsavir, lenacapavir

PI = protease inhibitor

DHHS. HIV Treatment Guidelines. Clinical Info HIV.gov Website. 2022. <https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf>. Spivack S, et al. *Drugs Context*. 2022;11:2021-9-1.

Patient Case: Final Thoughts



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CME OUTFITTERS

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Use DHHS guideline recommended protocols for HIV testing and monitoring in all patients taking oral and injectable PrEP to achieve timely identification of breakthrough HIV and limit drug resistance.
- Initiate empiric ART using guideline recommended regimens in all patients with confirmed PrEP-breakthrough acute HIV infection.
- Implement ART switching strategies based on drug history and resistance testing to overcome drug resistance in patients with HIV.

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1

HIV & SUD: Addressing
Barriers to Viral Suppression

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2

Team Approach to Addressing
Comorbidities in Aging
Populations of PLWH

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3

ART for PLWH Who Are Pregnant
or of Childbearing Potential

www.CMEOutfitters.com/infectious-disease-hub/

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Participants will be able to download and print their certificate immediately upon completion.