AETC AIDS Education & Training Center Program
Southeast Regional Conference 2023

# ART Modification/Evaluation Case-Based Panel

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Elizabeth Sherman, PharmD

# Disclosures

- *Dr. Leedy has no conflicts of interest to disclose*
- *Dr. Person has no conflicts of interest to disclose*
- *Dr. Felzien has no conflicts of interest to disclose*
- *Dr. Sherman has no conflicts of interest to disclose*

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# Speaker Bios

- Nicole Leedy, MD is an Associate Professor of Medicine at the University of Kentucky. She serves as the Infectious Disease Fellowship program director and faculty for Kentucky AETC.
- Anna Person, MD is an Associate Professor of Medicine at Vanderbilt University Medical Center. She serves as the IPE Director for the SE AETC.
- Gregory “Grey” Felzien, MD AAHIVS is the Medical Director of Positive Impact Health Center in Georgia.
- Elizabeth Sherman, PharmD is an HIV Clinical Pharmacist for the Memorial Healthcare System Division of Infectious Disease and an Associate Professor of Pharmacy Practice at Nova Southeastern University in Ft. Lauderdale, FL

# Objectives

- Discuss Less Stigmatizing Language
- Outline care for a highly treatment experienced individual
- Describe a patient on initial ART experiencing weight gain,
- Summarize a patient with loss of virologic control in the setting of optimal adherence and no resistance.

# Language

- Avoid using terminology that is stigmatizing
  - I.e. person is HIV positive or negative
  - ""… just as we don't describe people with cancer as "cancerous people," it is preferable to avoid labeling people with HIV as "HIV-positive people" and instead use more empowering language, such as "people living with HIV."
- Avoid using the terms AIDS, full blown AIDS, AIDS test
  - AIDS (stage-3 HIV is a syndrome)
- Consider other terminology
  - Promiscuous: use multiple partners, partner(s)
- Avoid discriminatory terminology
  - Drug addict / abuser: use person with a substance use disorder
  - "This focuses the use of substances as a clinical diagnosis rather than labeling the individual in a stigmatizing/discriminatory way"


1. https://www.thebodypro.com/article/hiv-medicine-clinical-language-terminology
2. http://www.hiveonline.org/wp-content/uploads/2016/01/Anti-StigmaSign-Onletter1.pdf
3. https://www.thewellproject.org/hiv-information/why-language-matters-facing-hiv-stigma-our-own-words#Preferred%20Language
4. Words Matter - Terms to Use and Avoid When Talking About Addiction | National Institute on Drug Abuse (NIDA) (nih.gov)
5. What is AWARENESS? What does AWARENESS Mean? Define AWARENESS (Meaning & Definition Explained) - YouTube

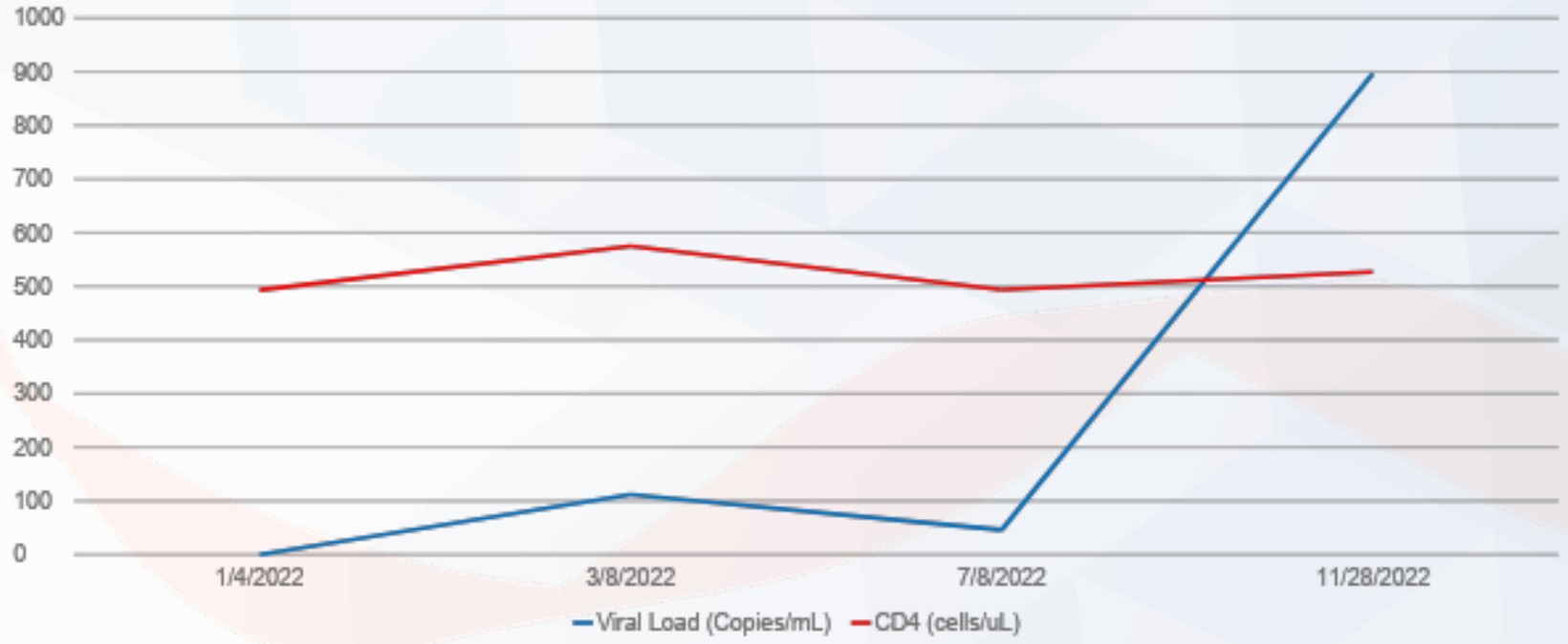
# Case #1: Dr. Leedy

45 yo F diagnosed with HIV in 1997 for follow up for viral breakthrough 12/2022.

- Increased work/home stressors with periods of incomplete adherence
- Current regimen (since 5/2021): DTG/3TC + DRV/c
- Tolerating well, no drug-drug interactions, no supplements.
- Engages in pharmacy driven pillbox fills

pexels.com

# HIV Lab Values Over Time



# ARV History

- Started ART in 2001, but records unavailable
- ? - 9/22/11: ZDV/3TC + ATV
- 9/22/11 - 12/2012: ABC/3TC + ETR + TPV/r + RAL
- 12/2012 - 4/2013: ABC + EVG/c/FTC/TDF
- 4/2013 - 6/2013: off ART
- 6/2013 - 11/2013: TDF + ABC/3TC + DRV/r
- 11/2013 - 7/2014: TDF + RAL + DRV/r
- 7/2014 - 4/2015: TDF/FTC + DTG + MVC
- 4/2015 - 12/2015: EVG/c/FTC/TDF + MVC
- 12/2015 - 11/2016: EVG/c/FTC/TDF + DRV
- 11/2016 - 4/2018: DRV/c + DTG + RPV
- 4/2018 - 5/2018: TAF/FTC + DRV/c + DTG
- 5/2018 - 5/2021: 3TC + DRV/c + DTG
- 5/2021 - present: DTG/3TC + DRV/c

# ARV Mutations

- 2/17/05: RT - K103N; PI - M36I
- 5/19/11: RT - M184V, K103S; PI - L10I, V32I, E35D, M36I, G73S, I85V, A71T
- 5/18/13: RT - K103N, VI06I; PI - E35D, M36I
- 6/23/13: INSTI (EVG/RAL) - none
- 6/4/14: RT - K103N, V106I; PI - K20K/R, E35D, M36I; INSTI (EVG/RAL/DTG) - none; Trofile - R5
- 10/15/14: INSTI - none
- 10/17/14: Trofile - R5
- 10/23/14: RT - K103N, V106I; PI - E35D, M36I
- 8/21/15: RT - K103N, V106I; PI - E35D, M36I
- 10/5/15: RT - K103N, V106I; PI - E35D, M36I
- 11/30/22: RT - M184V, T215D, K103S, E138Q, Y181C; PI - none; INSTI - E138K, S147G, N155H, R263K

# HIV Mutation Addition

| Nucleoside Reverse Transcriptase Inhibitors | |
|---|---|
| **abacavir (ABC)** | Low-Level Resistance |
| **zidovudine (AZT)** | Susceptible |
| **emtricitabine (FTC)** | High-Level Resistance |
| **lamivudine (3TC)** | High-Level Resistance |
| **tenofovir (TDF)** | Susceptible |

| Non-nucleoside Reverse Transcriptase Inhibitors | |
|---|---|
| **doravirine (DOR)** | Potential Low-Level Resistance |
| **efavirenz (EFV)** | High-Level Resistance |
| **etravirine (ETR)** | Intermediate Resistance |
| **nevirapine (NVP)** | High-Level Resistance |
| **rilpivirine (RPV)** | High-Level Resistance |

| Integrase Strand Transfer Inhibitors | |
|---|---|
| **bictegravir (BIC)** | High-Level Resistance |
| **cabotegravir (CAB)** | High-Level Resistance |
| **dolutegravir (DTG)** | High-Level Resistance |
| **elvitegravir (EVG)** | High-Level Resistance |
| **raltegravir (RAL)** | High-Level Resistance |

Stanford HIV Database; hivdb.stanford.edu

Current Regimen: DTG/3TC + DRV/c

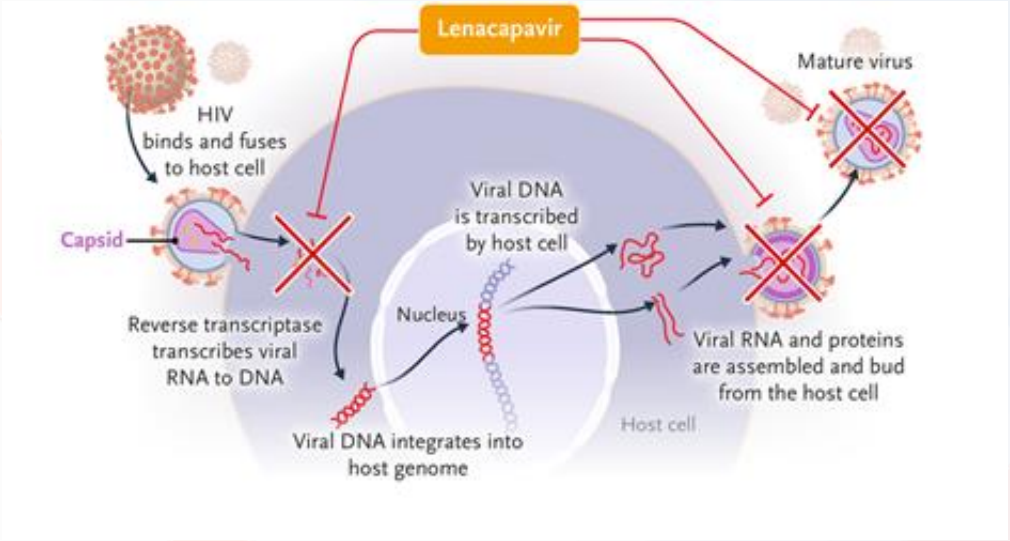
# Let's Make a Regimen!

A. Continue current regimen and wait for a new drug to be approved
B. Hold current regimen and wait for a new drug to be approved
C. DTG/3TC + DRV/c + FTR
D. DTG/3TC +DRV/c + Ibalizumab
E. DTG/3TC +DRV/c + LEN
F. TAF/FTC +DRV/c + FTR
G. TAF/FTC +DRV/c +Ibalizumab
H. TAF/FTC +DRV/c +LEN
I. Something else…

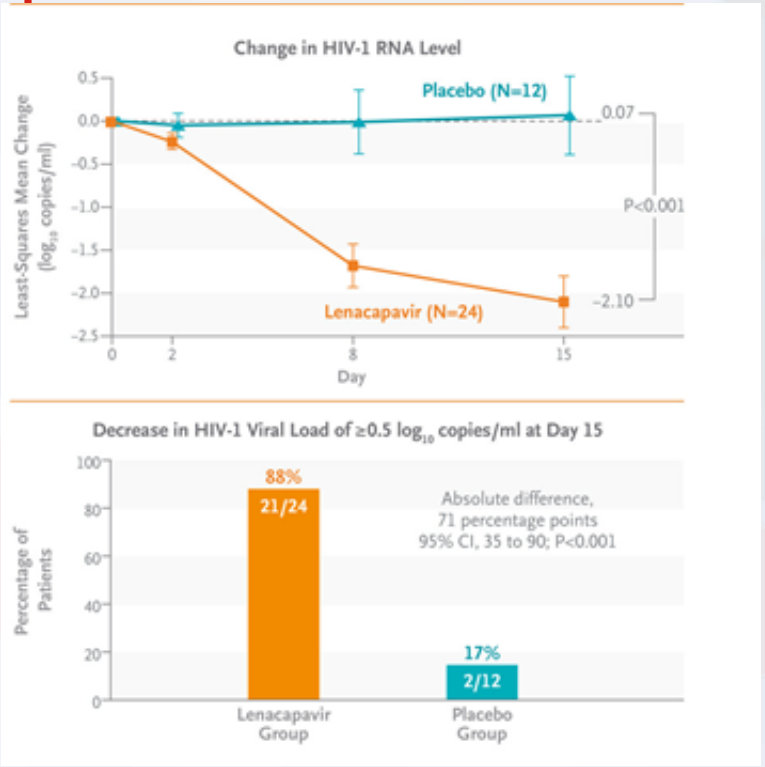
# What Happened

- Initiated on TAF/FTC + DRV/c + FTR
  - Unable to take medication: nausea and vomiting despite food w/meds
  - Significant anxiety: held meds
  - Minimal help with antiemetics
  - Would prefer to avoid infusions
- Transitioned to TAF/FTC +DRV/c +LEN
  - Tolerated well
  - CD4 stable
  - VL undetectable

# Lenacapavir (LEN): Novel Capsid Inhibitor




Segal-Maurer S et al. DOI: 10.1056/NEJMoa2115542

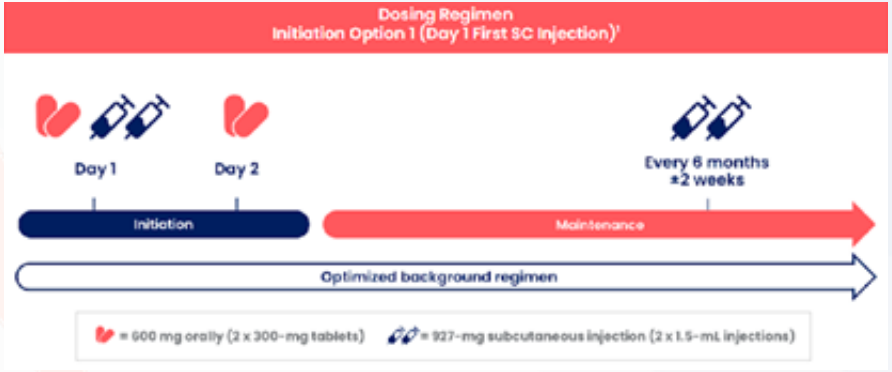


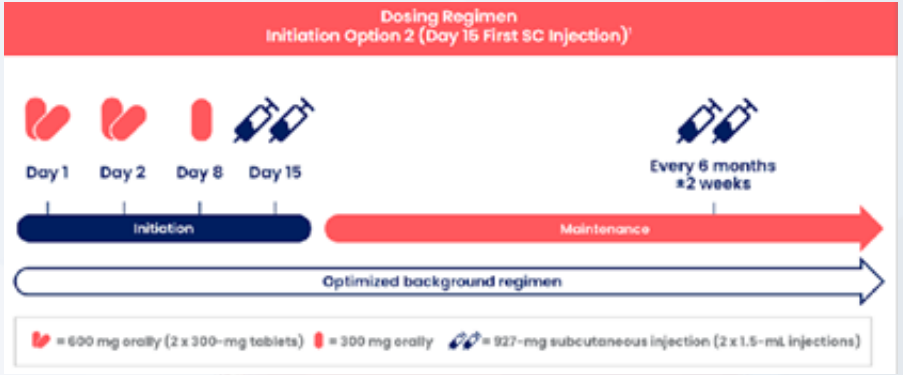

Indications: In combination with HIV background therapy in highly ARV experienced patients



Segal-Maurer S et al. NEJM 2022; 386:1793-1803

# Lenacapavir(LEN): Dosing




No dosage adjustment necessary in renal insufficiency
No hepatic dosing adjustment
CYP3A4 inhibitor (moderate)
Adverse reactions: injection site reactions, nausea, vomiting, diarrhea

Adapted from Gilead: https://www.sunlencahcp.com/. Accessed 9 August 2023

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. Year. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed (9 August 2023) [Appendix B, Table 11].

# Lenacapavir: Selected Drug-Drug Interactions

- Rifamycin antibiotics
- Anticonvulsants
  - Carbamazepine
  - Phenobarbital
  - Phenytoin
- Cardiac
  - Amiodarone
  - Quinidine
  - Digoxin
- Supplements
  - St. John's Wort

- ARVs
  - NNRTIs (↓LEN)
    - EFV
    - ETR
  - Protease Inhibitors (↑LEN)
    - ATV
    - ATV/r
    - ATV/c



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. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed (9 August 2023) [Table 24g].

# Case #2

"Doc, I've gained so much weight since I first started my medicine…"

47 year old woman with 22 lb weight gain since starting DTG +FTC/TAF 15 months ago. She does not have hepatitis B. She has normal renal function. Initial GT was wildtype.

- BMI from 26 to 31.
- A1c from 6.0 to 6.5.
- Initial CD4 count 250 cells/mm3, VL 84,000 copies/mL.
- Now CD4 count 620 cells/mm3, VL <20 copies/mL

What would you do?

# Weight Gain in ART

What would you do?

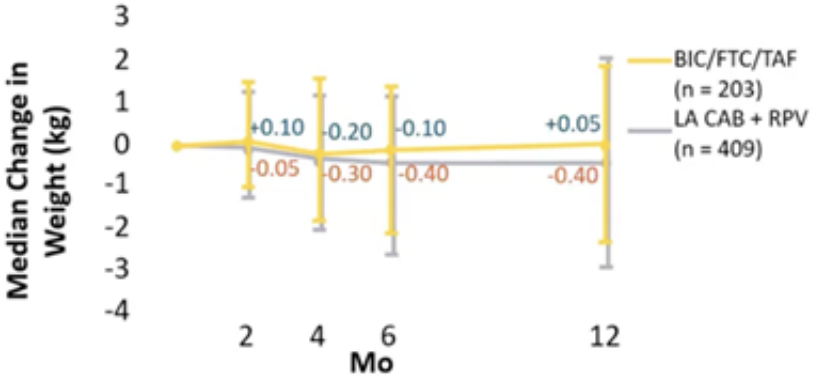
1) Assume this is a “return to health” phenomenon and refer her to your dietician.
2) Change ART to doravirine/FTC/TDF.
3) Start semaglutide.
4) Change to DTG + DRV/c.
5) Change to CAB + RIL.

# Weight Gain on ART

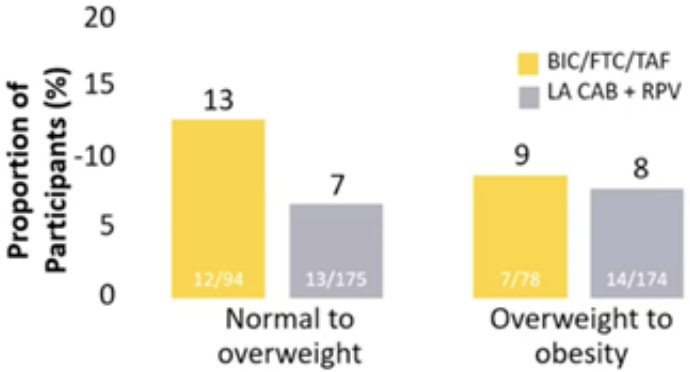


**SOLAR:** Randomized switch from BIC/FTC/TAF to LA CAB + RIL with or without oral lead-in.

**Median (IQR) Change in Weight Through Mo 12**




**Proportion of Participants With an Upward BMI Shift Resulting in Overweight or Obesity at Mo 12**

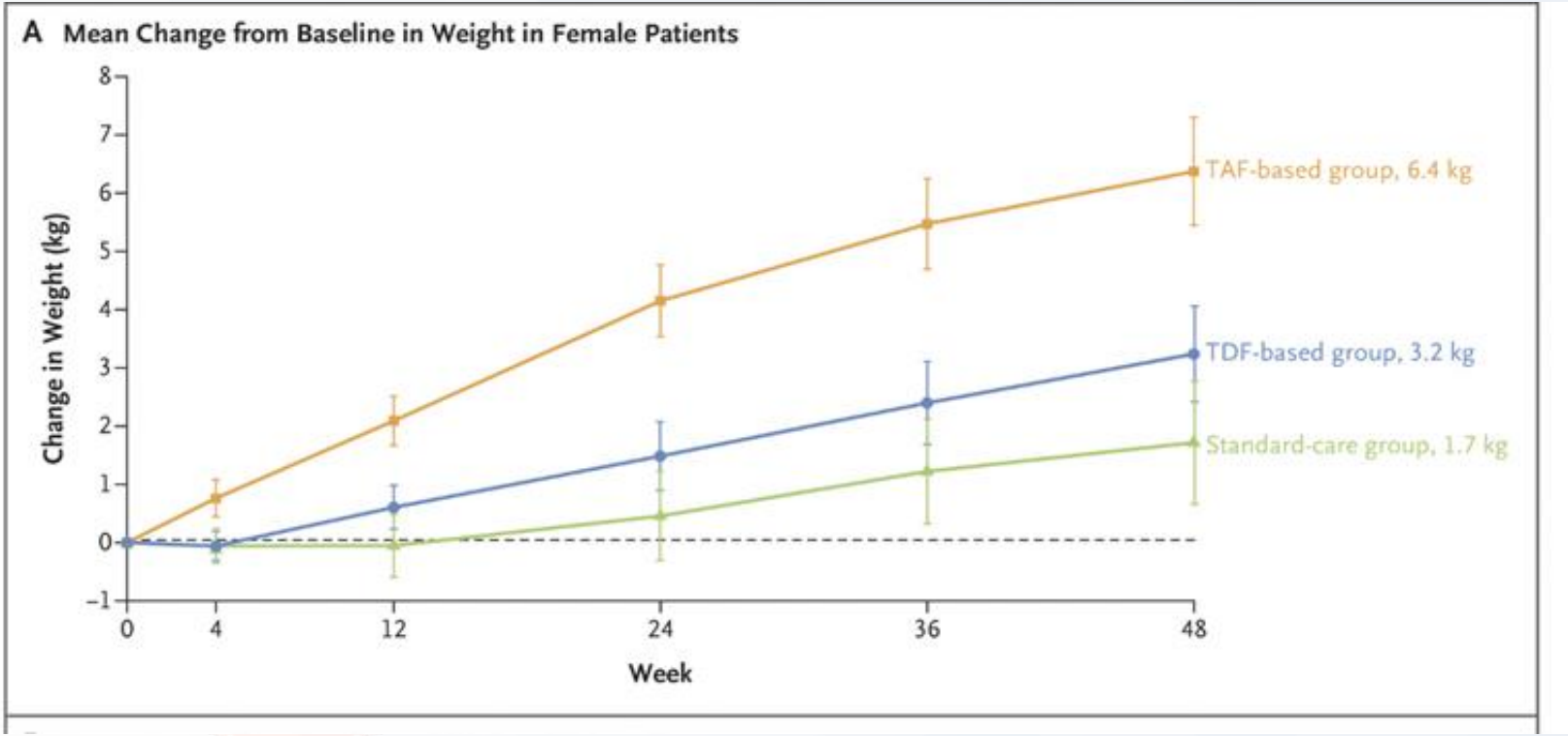



- **Very small decrease in weight for those who switched. Slightly more people went from normal BMI to overweight BMI in the bic group than the LA group.**
- No clinically relevant changes in hip or waist circumference or frequency of metabolic syndrome and insulin resistance between baseline and Mo 12 in either arm

Tan. CROI 2023. Abstr 146.

# Weight Gain on ART

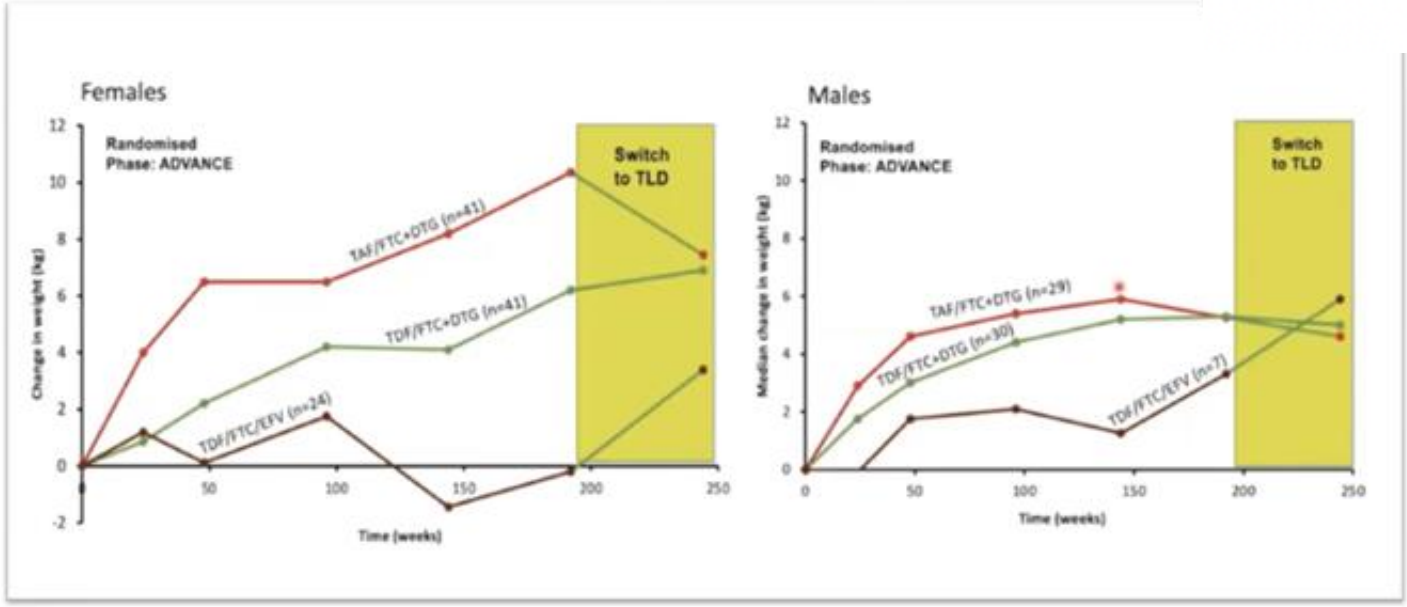
ADVANCE: Published in NEJM in 2019, RCT in S Africa of >1000 ART naive patients randomized to EFV/TDF/FTC, DTG/TAF/FTC or DTG/TDF/FTC.



# Weight Gain on ART



CHARACTERISE: All 3 groups from ADVANCE changed to DTG/3TC/TDF.




Some weight LOSS. How much is taking off TAF (associated with weight gain), vs switching to TDF (associated with weight loss in some studies). Giving hope that this can change? Particularly in women?

Bosch, et al. CROI 2023, Abst. 167

# A5391: Doravirine for Persons with Excessive Weight Gain on Integrase Inhibitors and Tenofovir Alafenamide (The Do IT Study)

# Weight Gain on ART: A5391

Enrollment criteria:

- People living with HIV-1 who are at least 18 years of age
- Currently on an Integrase Inhibitor (INSTI) containing regimen (bictegravir, dolutegravir or raltegravir) plus TAF/FTC (or TAF/3TC) for at least 48 weeks
- HIV viral load less than 50 copies
- Have a body mass index (BMI) at least 30 kg/m2.
- No plans to undergo weight loss surgery or to start significant exercise, diet, or medications affecting weight (e.g., structured weight loss programs such as Weight Watchers)

# Weight Gain on ART: A5391

Participants will be randomized to one of three study groups:

Group 1: DOR and continue taking TAF/FTC (or TAF/3TC)

Group 2: DOR and switch TAF to TDF/FTC (or TDF/3TC)

Group 3: Continue current INSTI+TAF/FTC (or TAF/3TC)

# Weight Gain on ART



So…. given these data, what would you do for our patient?

“47 year old woman with 22 lb weight gain since starting DTG +FTC/TAF 15 months ago. She does not have hepatitis B. She has normal renal function. Initial GT was wildtype.

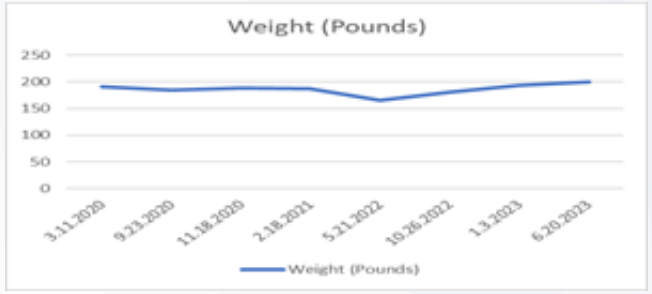
- BMI from 26 to 31.
- A1c from 6.0 to 6.5.
- Initial CD4 count 250 cells/mm3, VL 84,000 copies/mL.
- Now CD4 count 620 cells/mm3, VL <20 copies/mL”

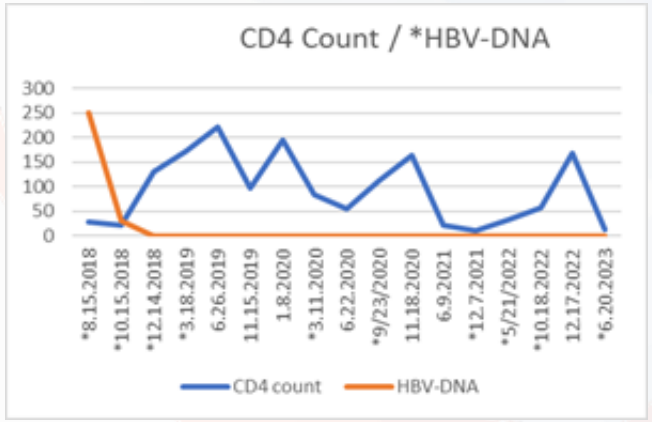
# Case #3: Dr. Felzien

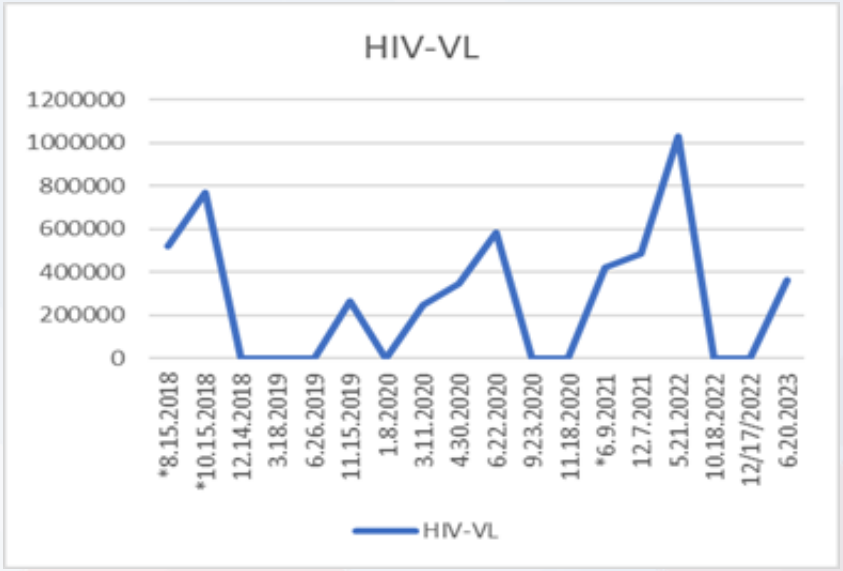
51yo AAF initially seen in consultation June 2023 for persistent HIV-VL elevation

- HIV/HBV diagnosis: 2018 — Genotype May 2018: V82I
  - Initial ARV: Genvoya™
- Continued HIV-VL elevation — Genotype Sept. 2018: V82I
  - Sept: 2018: Switch to Biktarvy™
- Continued HIV-VL elevation — Geno June 2021: L178M, Q207E, L283I, V82I
  - July 2021: Added Prezcobix™ to Biktarvy™
- All: Bactrim/Dapsone — Meds: Atovaquone, Cetirizine

# CD4 Count, HIV/HBV Viral Loads & Weight




* Genotype testing

*8/15/2018: 1,830,000

# Stanford HIV Database

| Nucleoside Reverse Transcriptase Inhibitors | |
|---|---|
| abacavir (ABC) | Susceptible |
| zidovudine (AZT) | Susceptible |
| stavudine (D4T) | Susceptible |
| didanosine (DDI) | Susceptible |
| emtricitabine (FTC) | Susceptible |
| lamivudine (3TC) | Susceptible |
| tenofovir (TDF) | Susceptible |

| Non-nucleoside Reverse Transcriptase Inhibitors | |
|---|---|
| doravirine (DOR) | Susceptible |
| efavirenz (EFV) | Susceptible |
| etravirine (ETR) | Susceptible |
| nevirapine (NVP) | Susceptible |
| rilpivirine (RPV) | Susceptible |

| Protease Inhibitors | |
|---|---|
| atazanavir/r (ATV/r) | Susceptible |
| darunavir/r (DRV/r) | Susceptible |
| fosamprenavir/r (FPV/r) | Susceptible |
| indinavir/r (IDV/r) | Susceptible |
| lopinavir/r (LPV/r) | Susceptible |
| nelfinavir (NFV) | Susceptible |
| saquinavir/r (SQV/r) | Susceptible |
| tipranavir/r (TPV/r) | Susceptible |

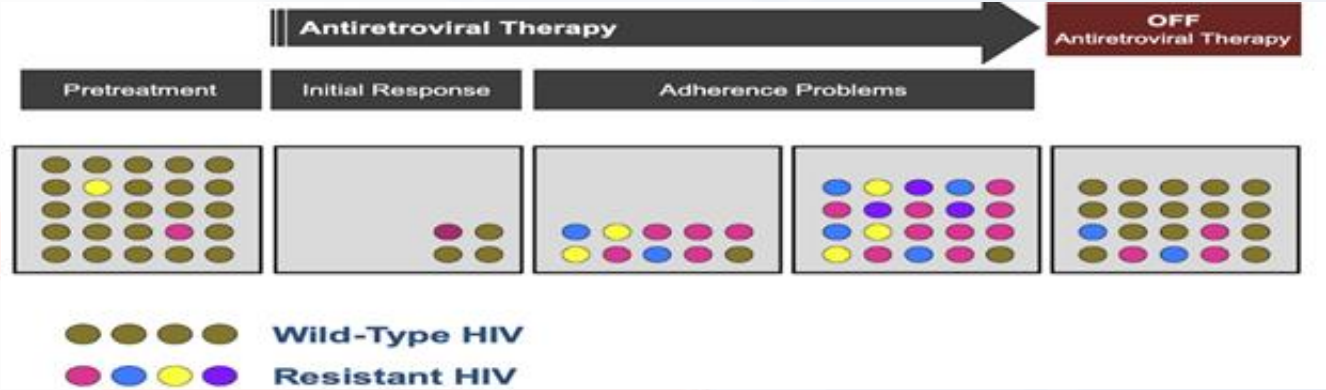
Mutations: I178M, Q207E, L283I, V82I

hivdb.stanford.edu

# Genotype Testing



- Genotype Assay: require a plasma viral load of at least 500-1,000 copies/mL
  - Drug-resistant viruses constituting <10-20% of circulating virus will probably not be detected
  - Wild-type virus often re-emerges (4-6 weeks) as the predominant population after ARV discontinuation
  - Selective pressure on drug-resistant virus stops & virus with resistant mutations drops to below 10-20%
- Archived Genotype: analyzes & detects HIV-1 proviral DNA below 500 copies/mL
  - May miss some or all previously existing drug-resistance mutations
  - usefulness of these assays in the clinic is still under investigation

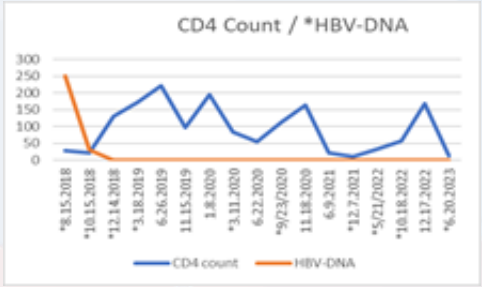



Drug-Resistance Testing | NIH (hiv.gov)

Core Concepts - Evaluation and Management of Virologic Failure - Antiretroviral Therapy - National HIV Curriculum (uw.edu)

# Hepatitis B

- Initial HBV-DNA: 1,830,000 with all follow-up levels undetectable
- Updated HBV labs pending: most recent with sAg & Core Ab: Positive
- AST: 32 / ALT: 21, Tot. Bili: 0.3, Plt: 121K




- Question if adherence is the main issue:
  - HBV conversion to immune state?
  - Chronic Inactive HBV
    - HBsAg present for ≥6 months
    - eAg (-) / eAb (+) [historically not available for case: pending recent labs]
    - HBV DNA <2000
    - Persistently normal AST/ALT

# Next Steps?

- Discussion with client and family
  - Client describes taking HIV medications the same time daily
  - Client states that medications are picked up from the pharmacy on-time
  - Family, when present, states they see the client taking medications

- Discussion/Ideas with/from care team
  - Pharmacy confirms medications being picked up consistently & on time
  - Team recommendation
    - More contact with client to minimize gaps in service (phone, tele-, office)
    - DOT via tele-services
    - Use of Long-acting Injectables
    - Testing for ARV drug levels

# Long Acting Injectables

- Sunlenca™ (Lenacapavir)
  - HIV-1 infection in heavily treatment-experienced adults
  - SQ ARV used in combination with ORAL medications

- Cabenuva™ (CAB:Cabotegravir/Rilpivirine)
  - HIV-1 infection in adults to replace current ARV regimen
  - Virologically suppressed (<50 copies/mL) & no know CAB resistance

  - What does the Literature say? (not FDA approved)
    - 24 patients virally suppressed (median CD4: 706), 100% maintained viral suppression
    - 15 patients with detectable viremia (median CD4: 99; mean $\log_{10}$ viral load, 4.67
      - 12 (80%) achieved viral suppression
      - 3 had a 2-log viral load decline by a median of 22 days

sunlenca_pi.pdf (gilead.com)
LABEL (fda.gov)
First Demonstration Project of Long-Acting Injectable Antiretroviral Therapy for Persons With and Without Detectable Human Immunodeficiency Virus (HIV) Viremia in an Urban HIV Clinic | Clinical Infectious Diseases | Oxford Academic (oup.com)

# Ursure/Orasure Care Team Question



UrSure

[OraSure Technologies, Inc. Announces Purchase of UrSure, Inc.](#) (May 2020

OraSure Technologies

**SHORT TERM POINT OF CARE TESTING**

**Requires IRB with Company**

**LONG-TERM ADHERENCE TESTING**

Measures levels of tenofovir-diphosphate

**Requires MOU with Molecular Testing Labs**

Still in studies for HIV-PrEP only

[Home | UrSure, Inc. (ursureinc.com)](#)
[Objective Adherence Monitoring (orasure.com)](#)

NEXT STEPS

# Thoughts from the Group / Update

Do thoughts even matter? - Three Principles Living (three-principles.com)



Expressing Your Gratitude Is More Powerful Than You Think – Arizona Daily Independent
Questions or Comments for GNI - Good Neighbor Insurance (gninsurance.com)

# AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinical Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu