Interactive ART Cases From the Clinic(ians): Case-Based Panel Discussion

Michael S. Saag, MD

Professor of Medicine

University of Alabama at Birmingham

Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Saag has received research grants and support awarded to his institution from Gilead Sciences, Inc and ViiV Healthcare. Dr Saag is a consultant for TFF Pharmaceuticals and AmericanGene Technologies. (Updated 10/8/22)

Learning Objectives

After attending this presentation, learners will be able to assess and select antiretroviral therapy (ART) in patients who:

- Are starting initial therapy
- Have ART-associated weight gain
- Are or plan to become pregnant
- Have a virologic blip
- Have a discordant CD4+ cell count response

Question

What regimen should I use as initial therapy?

Case 1

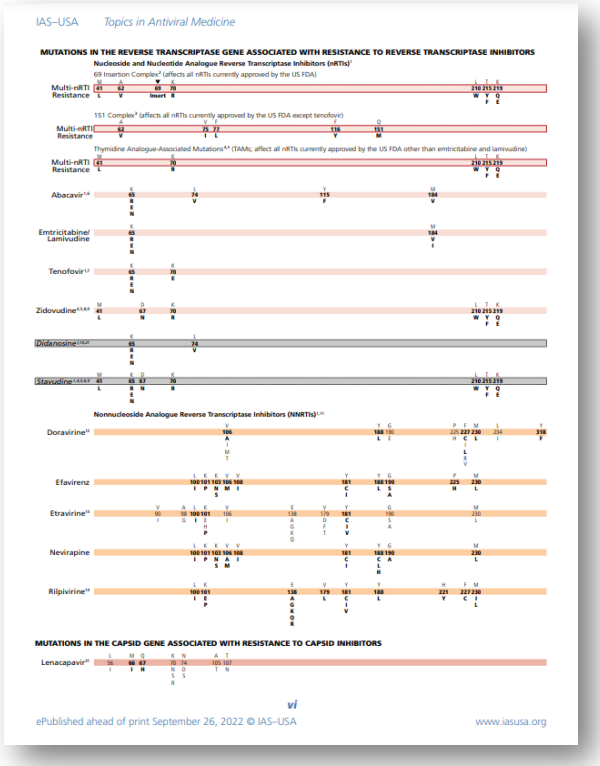
- 48 yo man presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial:** HIV RNA 280,000 c/ml
  CD4 count 65 cells/ul
- Other labs are normal
- Genotype is Wild-type virus
- No prior medical history. Normal renal function
- Okay to start therapy

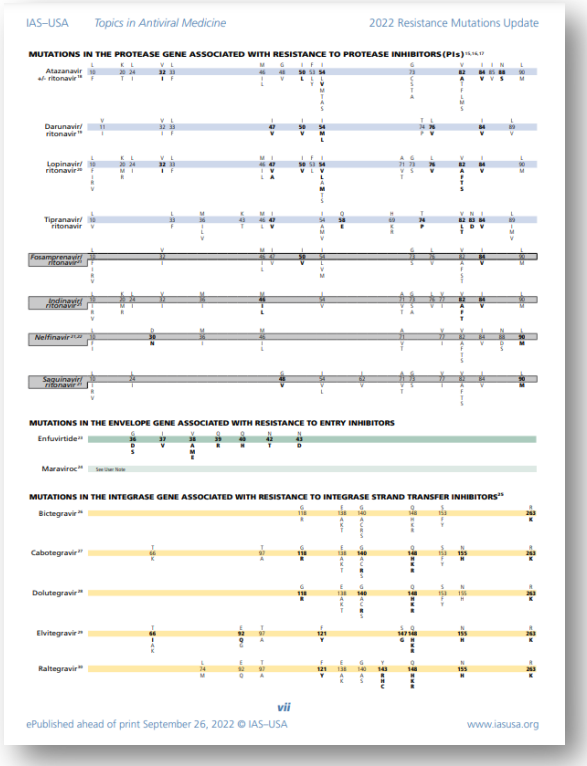
slido

Which regimen would you choose?

ⓘ Start presenting to display the poll results on this slide.

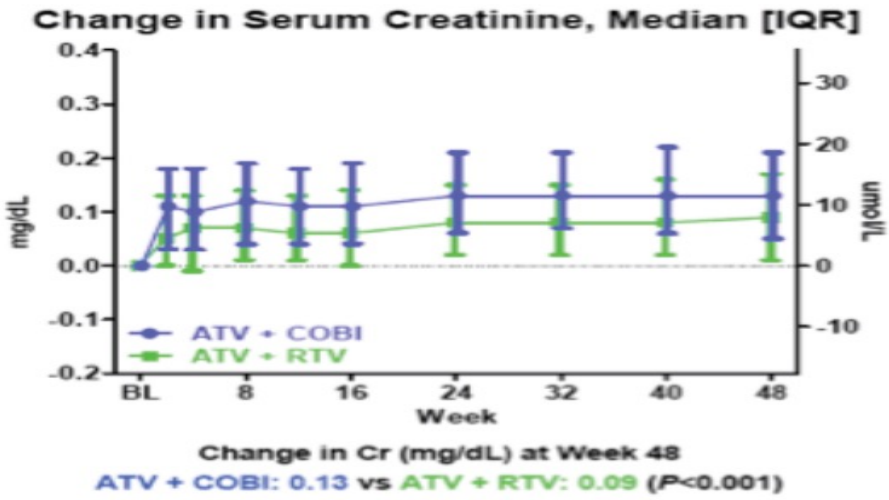
2022 Update of the Drug Resistance Mutations in HIV-1

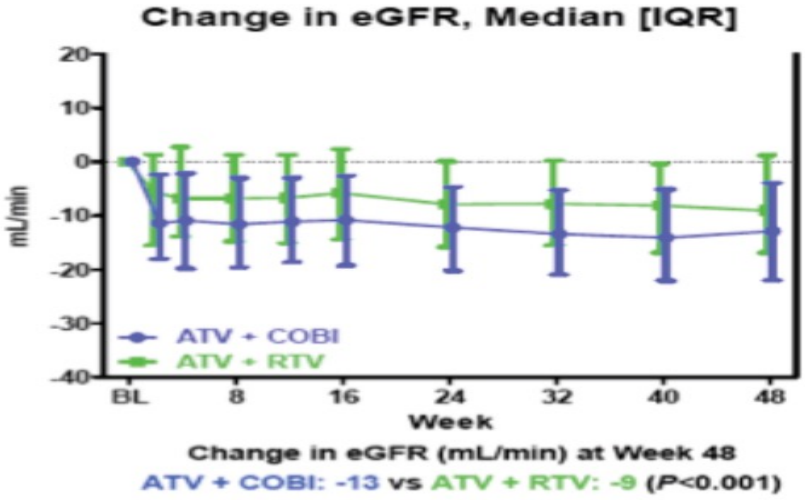




Now available on the IAS–USA website!

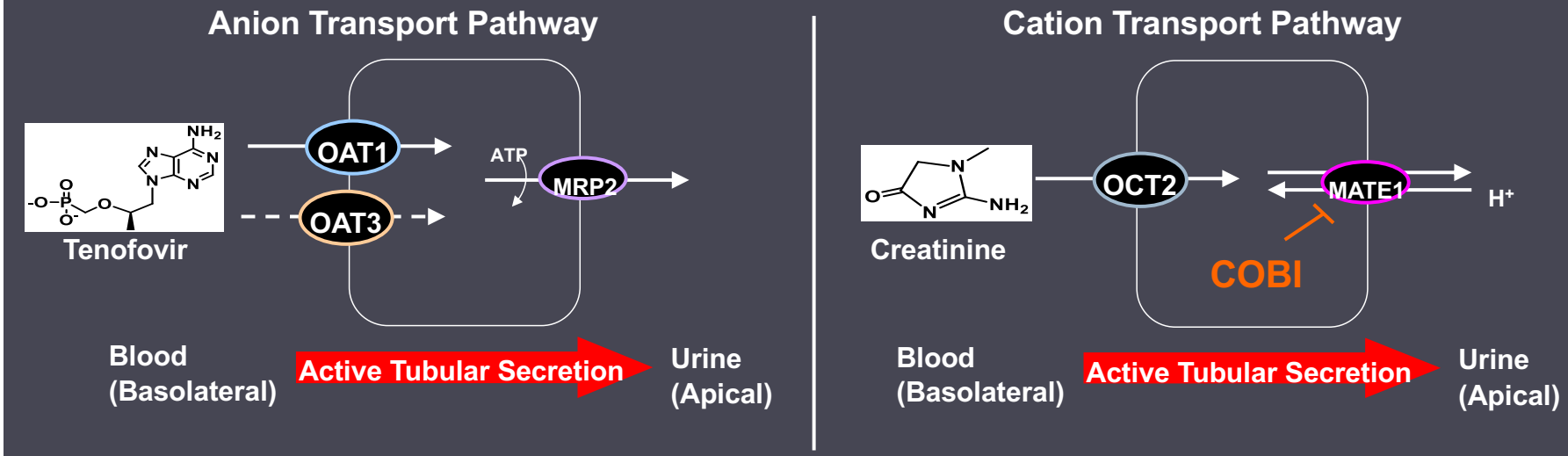
Changes in Serum Creatinine and eGFR





Gallant IAS 2012

Tenofovir and COBI Interact with Distinct Renal Transport Pathways



The active tubular secretion of tenofovir and the effect of COBI on creatinine are mediated by distinct transport pathways in renal proximal tubules

Ray A, et al. Antimicro Agents Chemo 2006;3297-3304
Lepist E, et al. ICAAC 2011; Chicago. #A1-1724

Question

What regimen should I use as initial therapy (3 years from now)?

ARS Question 2: Which regimen would you choose?

A. TAF/ FTC (fdc) + DTG
B. TAF/ FTC / BIC (fdc)
C. Cabotegravir + RPV IM every 8 weeks
D. Islatravir + Lenacapavir SQ q 6 mon
E. bNAB + (Leronlimab or Albuvirtide) SQ QOW
F. Implantable Lenacapavir + Islatravir q 12 months
G. Some other option….

- 48 yo man newly dx HIV
- Asymptomatic
- HIV RNA 280,000 c/ml
  CD4 65 cells/ul
- Other labs are normal
- Wild-type virus
- No prior medical history
- HBV immune
- Normal renal function
- Ok to start therapy

slido

Which regimen would you choose?

ⓘ Start presenting to display the poll results on this slide.

Question

Seems like we are now starting ARV therapy for about everyone, what about starting therapy for an **Elite Controller**?

Case 2

- 30 yo male was diagnosed with HIV infection 7 years ago
- Asymptomatic
- **Initial:** HIV RNA < 50 c/ml (HIV DNA positive)
  CD4 count 870 cells/ul

- Other labs are normal
- Genotype determined from DNA is wild-type

- No prior medical history.

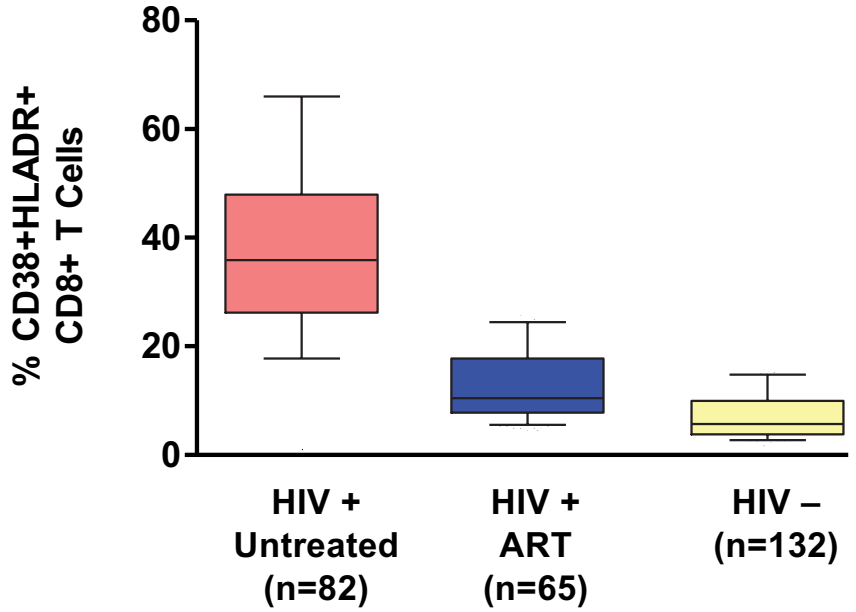
- Ok to start therapy if you think he should

slido

Would you start ARV Rx now?

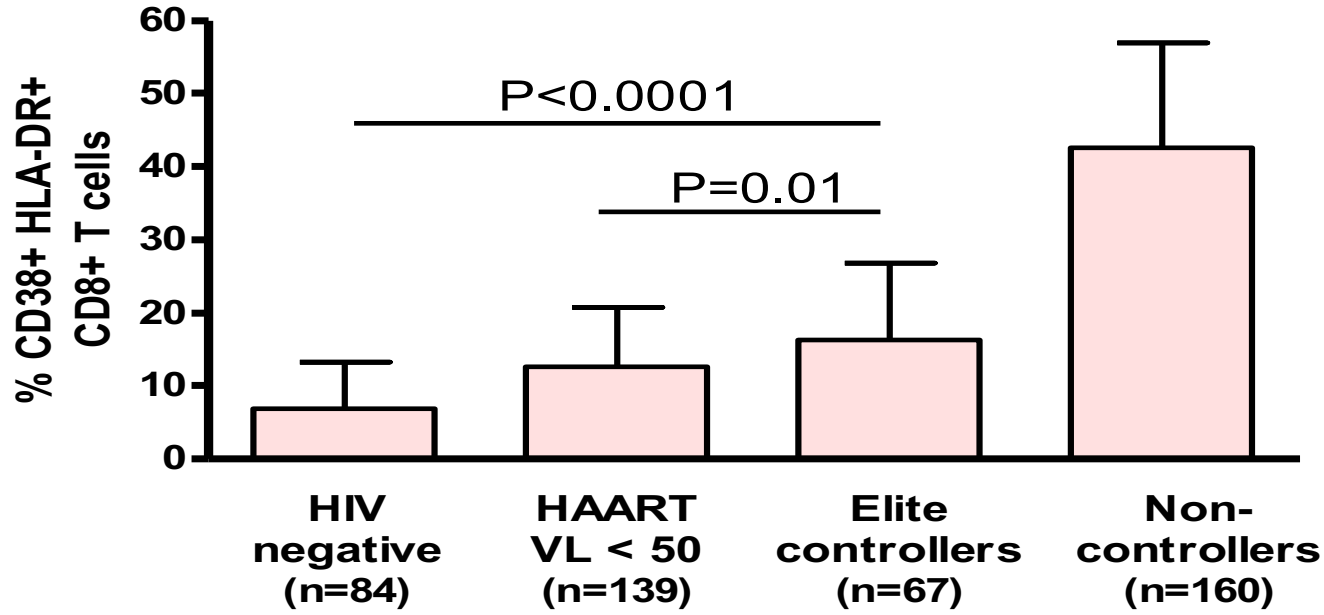
ⓘ Start presenting to display the poll results on this slide.

T cell "activation" is lower in treated than untreated adults, but consistently higher than "normal"



Hunt et al JID 2003, PLoS ONE 2011 and unpublished

Elite controllers have higher levels of CD8 "activation" than other aviremic groups, including those on HAART and HIV negatives



Activation higher in elites that other "aviremic" groups even after adjustment of CD4, age and other factors

Hunt JID 2008
(see also Lopez Abstract 366)

Question

How do I manage ‘blips’?

Case 3

- 48 yo man presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial:** HIV RNA 280,000 c/ml
  CD4 count 65 cells/ul
- He is started on Bic/TAF/FTC 2 years ago
- HIV RNA remained undetectable until:
  - 4 months ago: HIV RNA 91 c/ml
  - 2 months ago: HIV RNA 185 c/ml
  - 1 week ago: HIV RNA 220 c/ml

slido

He claims full adherence. Which of the following is the most likely cause of the virologic failure?

ⓘ Start presenting to display the poll results on this slide.

Question

How should ARV associated weight gain be managed?

Case 4

- 47 yo woman started BIC/FTC/TAF 12 months ago as her first regimen
- **Initial:** HIV RNA 28,000 c/ml (Wild-type virus)
  CD4 count 450 cells/ul
- **Current:** HIV RNA <20 c/mL / CD4+ count 930 /uL
- Since starting her current regimen her weight has increased from **145 lbs to 171 lbs**

slido

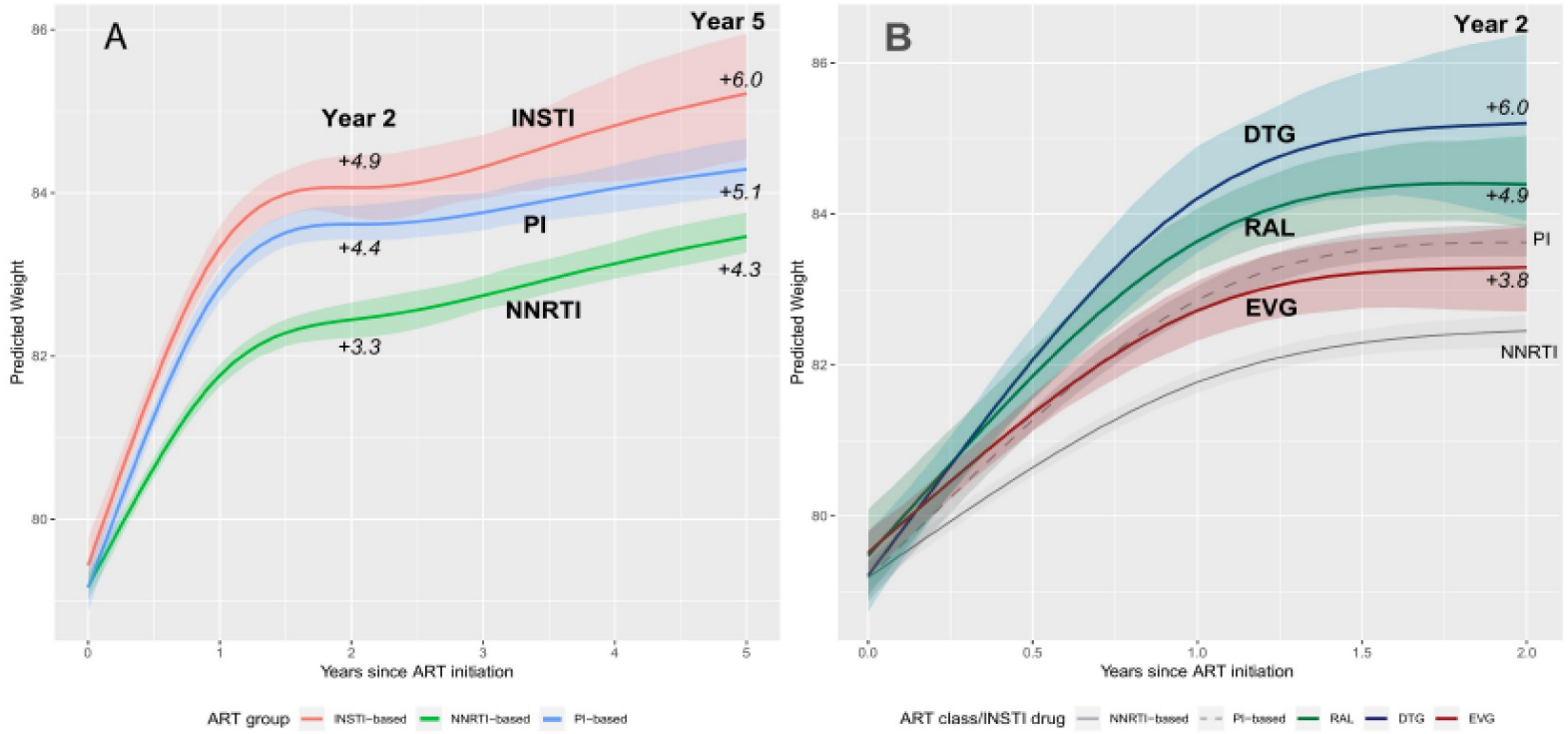
At this point you would

ⓘ Start presenting to display the poll results on this slide.

Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019

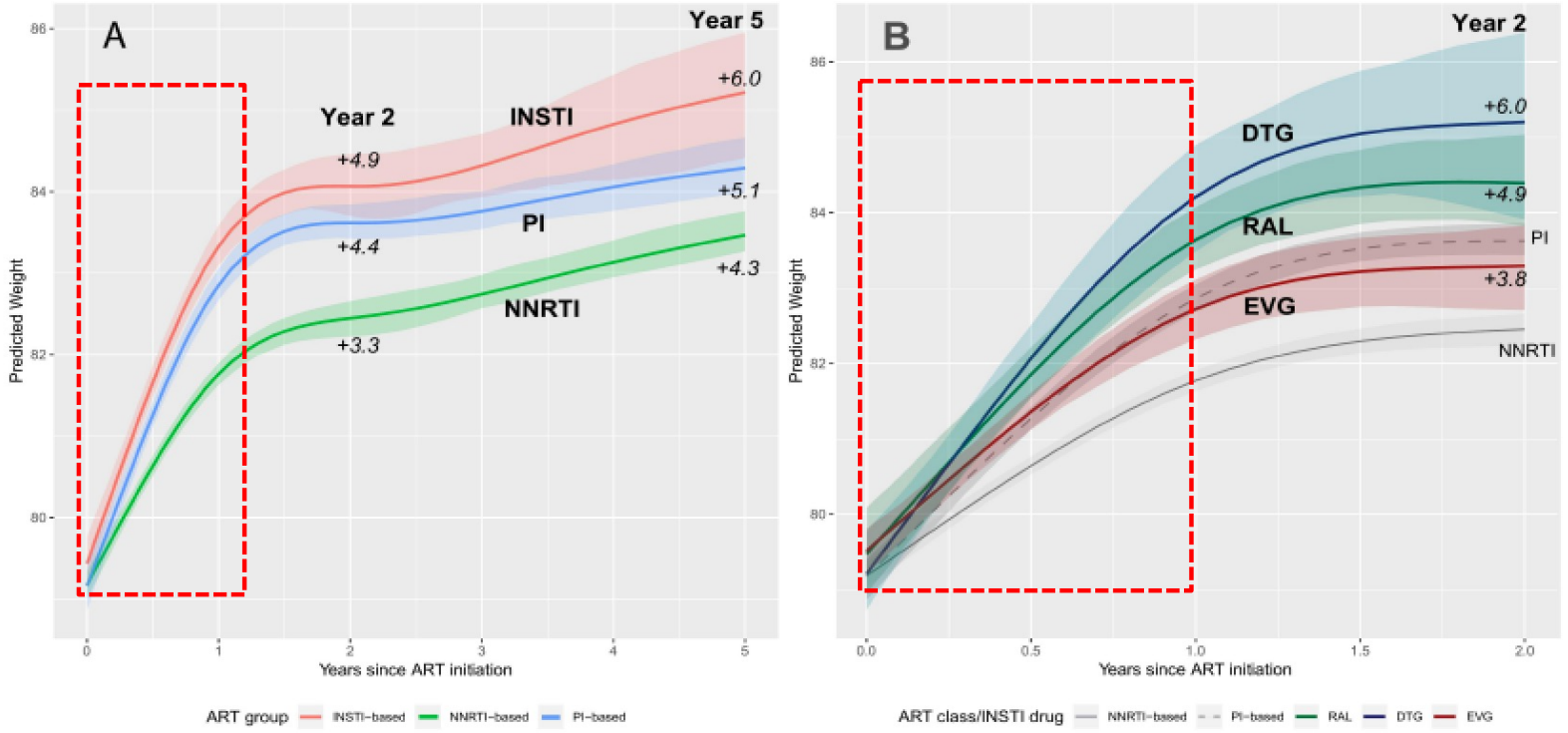
INSTI distribution: 4,740 Total; **1,681 (35%)** RAL; **2,124 (45%)** EVG; **935 (20%)** DTG



Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019

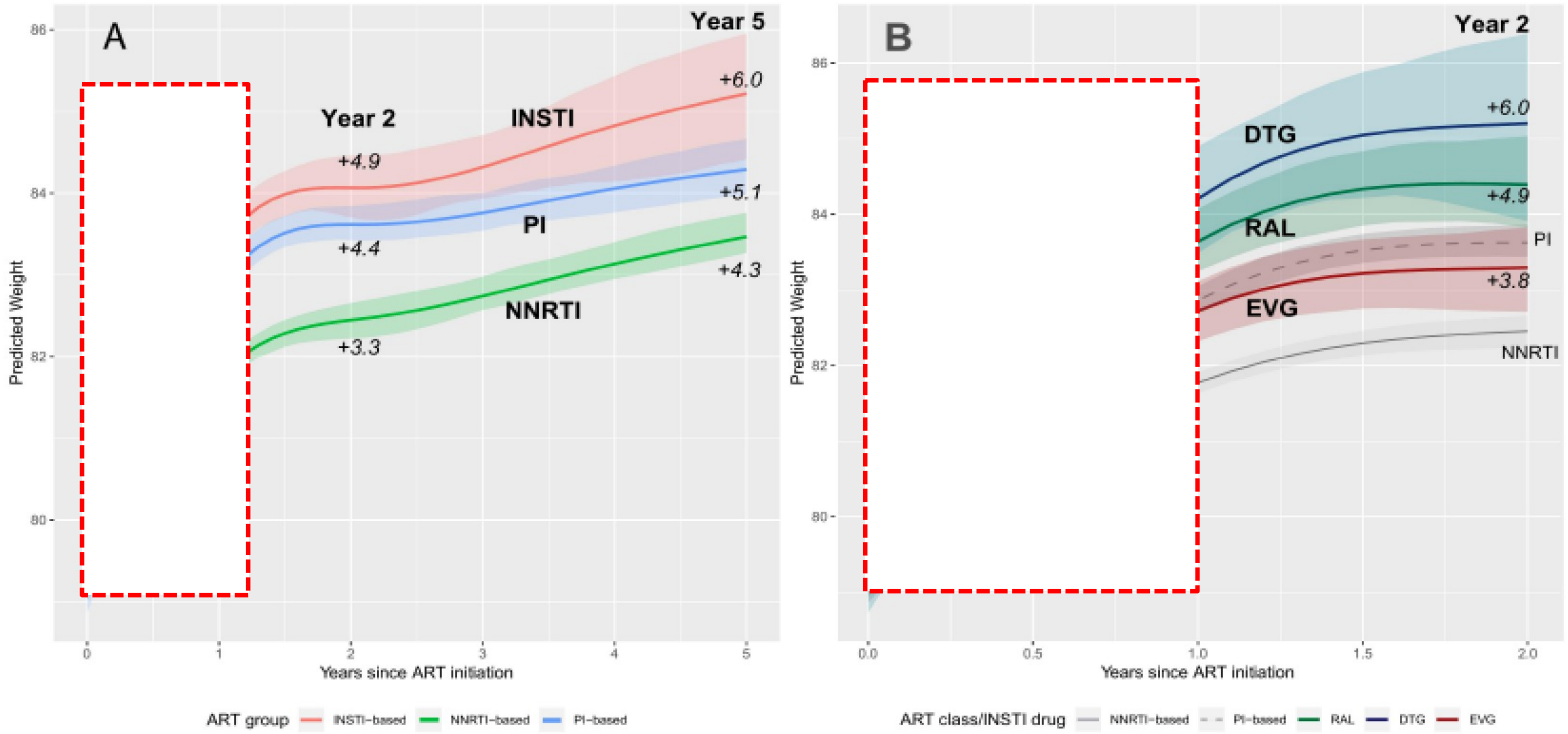
INSTI distribution: 4,740 Total; **1,681 (35%)** RAL; **2,124 (45%)** EVG; **935 (20%)** DTG



Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019

INSTI distribution: 4,740 Total; **1,681 (35%)** RAL; **2,124 (45%)** EVG; **935 (20%)** DTG



Question

What regimen should I use as initial therapy in a pregnant patient?

Case 5

- 30 yo woman presents with newly diagnosed HIV infection
- Asymptomatic, 6 weeks pregnant
- **Initial:** HIV RNA 28,000 c/ml
  CD4 count 650 cells/ul
- Other labs are normal; HLA-B*5701 neg
- Genotype is Wild-type virus
- No prior medical history. First pregnancy
- Ok to start therapy

slido

At this point which regimen would you choose?

ⓘ Start presenting to display the poll results on this slide.

DHHS Guidelines Dec 30, 2021: What to Start in Pregnancy

Two NRTIs

Abacavir/3TC or

TAF/FTC, TAF/3TC or

TDF/FTC, TDF/3TC

Bictegravir (limited data)
Elvitegravir/cobi (PK concerns)
DRV/cobi (PK concerns)
ATV/cobi (PK concerns)
DOR (no data)
Fostemsavir (limited data)
Oral or IM CAB/RPV (insufficient data)

Plus

Integrase inhibitor:

Raltegravir (twice daily) or

Dolutegravir

or

Protease inhibitor:

Darunavir/ritonavir (twice daily) or

Atazanavir/ritonavir

Slide per Dr. Raj Gandhi

Question

How do I simplify a complex regimen?

Case 6

- 55 yo man referred to you for evaluation
- Diagnosed 24 years ago with HIV infection
- **Initial:** HIV RNA 936,000 c/ml
  CD4 count 70 cells/ul
- **Current:** HIV RNA < 20 c/ml
- CD4 count 525 cells/ul
- Started on NEL/D4T/3TC; subsequently treated with
  - LOP-r / TDF/FTC
  - EFV/ FTC/ TDF (fdc)
  - Now **DTG / DRV/c / TAF / FTC**
- No historical resistance tests are available

slido

Should the Regimen be Changed?

ⓘ Start presenting to display the poll results on this slide.

Question

What do I do with a patient who has persistently detectable viremia?

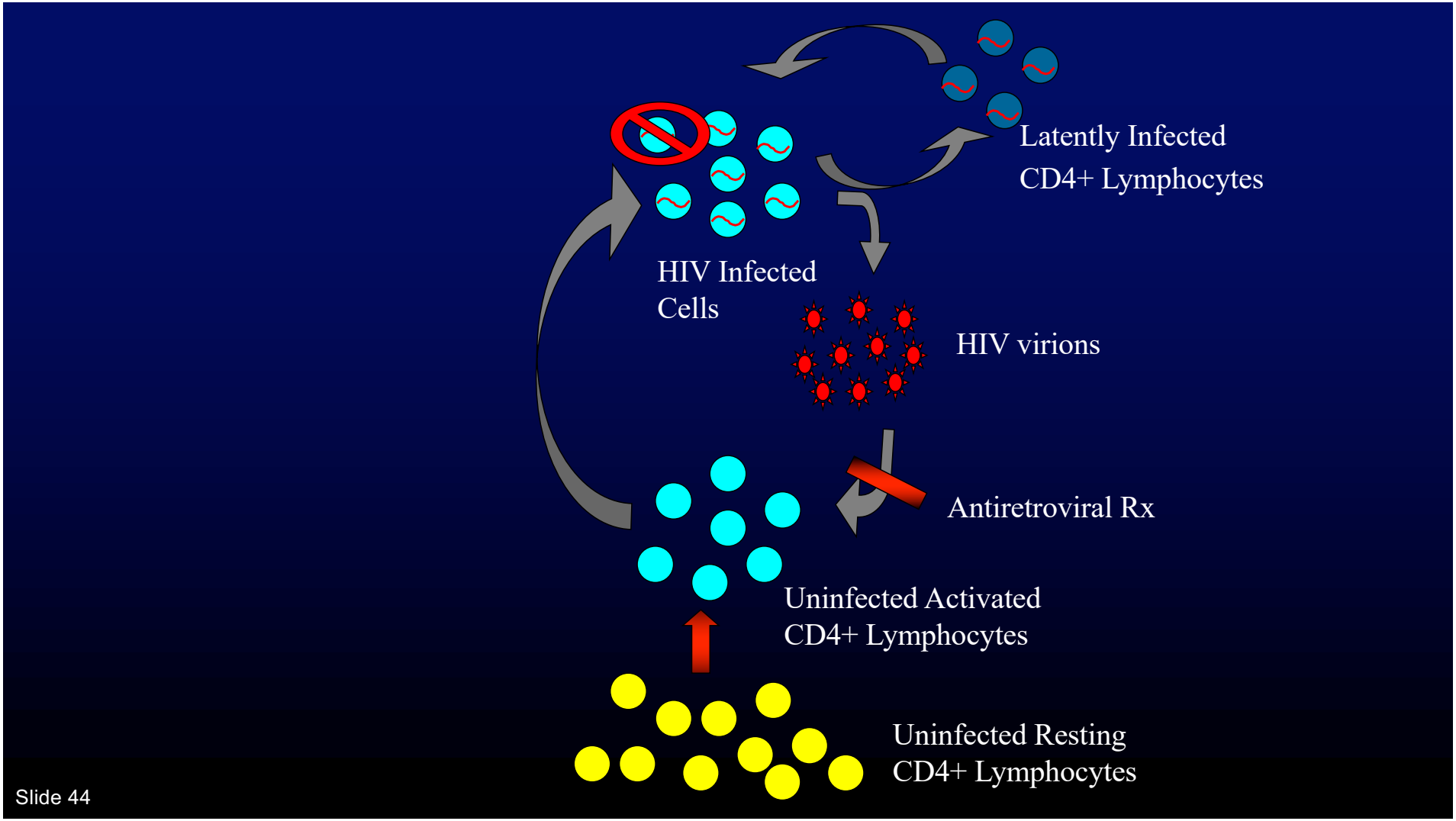
Case 7

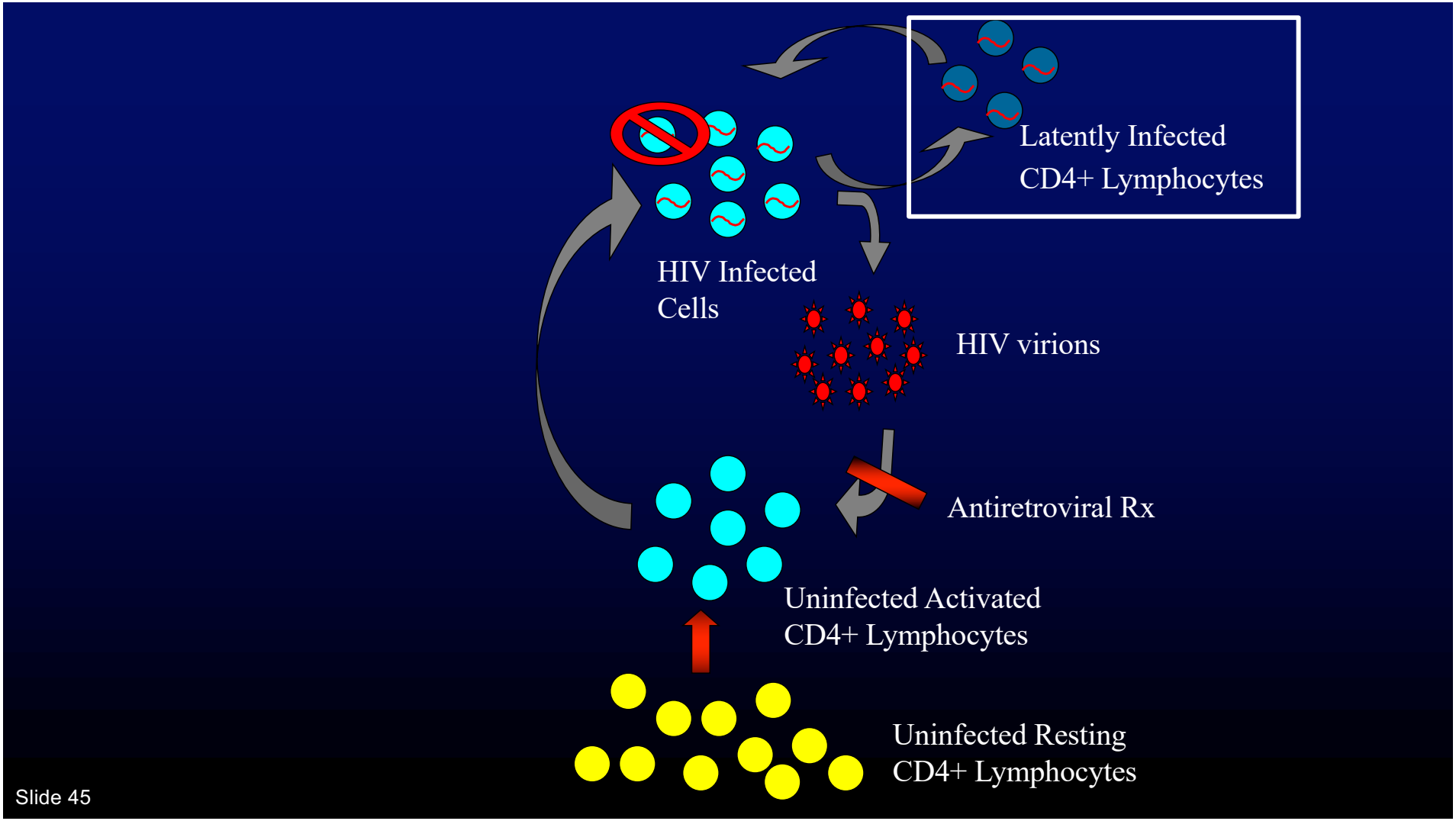
- 55 yo man referred to you for evaluation
- Diagnosed 18 years ago with HIV infection
- **Initial:** HIV RNA 936,000 c/ml
  CD4 count 70 cells/ul
- **Current:** HIV RNA 85 c/ml (prior value 62 c/ml)
  CD4 count 525 cells/ul
- Started on NEL/D4T/3TC; subsequently treated with
  - LOP-r / TDF/FTC
  - EFV/ FTC/ TDF (fdc)
  - Now **DTG / DRV/c / 3TC**
- No historical resistance tests are available

slido

Should you change ARV therapy now?

ⓘ Start presenting to display the poll results on this slide.


Latently Infected
CD4+ Lymphocytes
HIV Infected
Cells
HIV virions
Antiretroviral Rx
Uninfected Activated
CD4+ Lymphocytes
Uninfected Resting
CD4+ Lymphocytes


Latently Infected
CD4+ Lymphocytes
HIV Infected
Cells
HIV virions
Antiretroviral Rx
Uninfected Activated
CD4+ Lymphocytes
Uninfected Resting
CD4+ Lymphocytes

Question

What do I do with a patient who has a ‘discordant’ CD4 count response?

Case 8

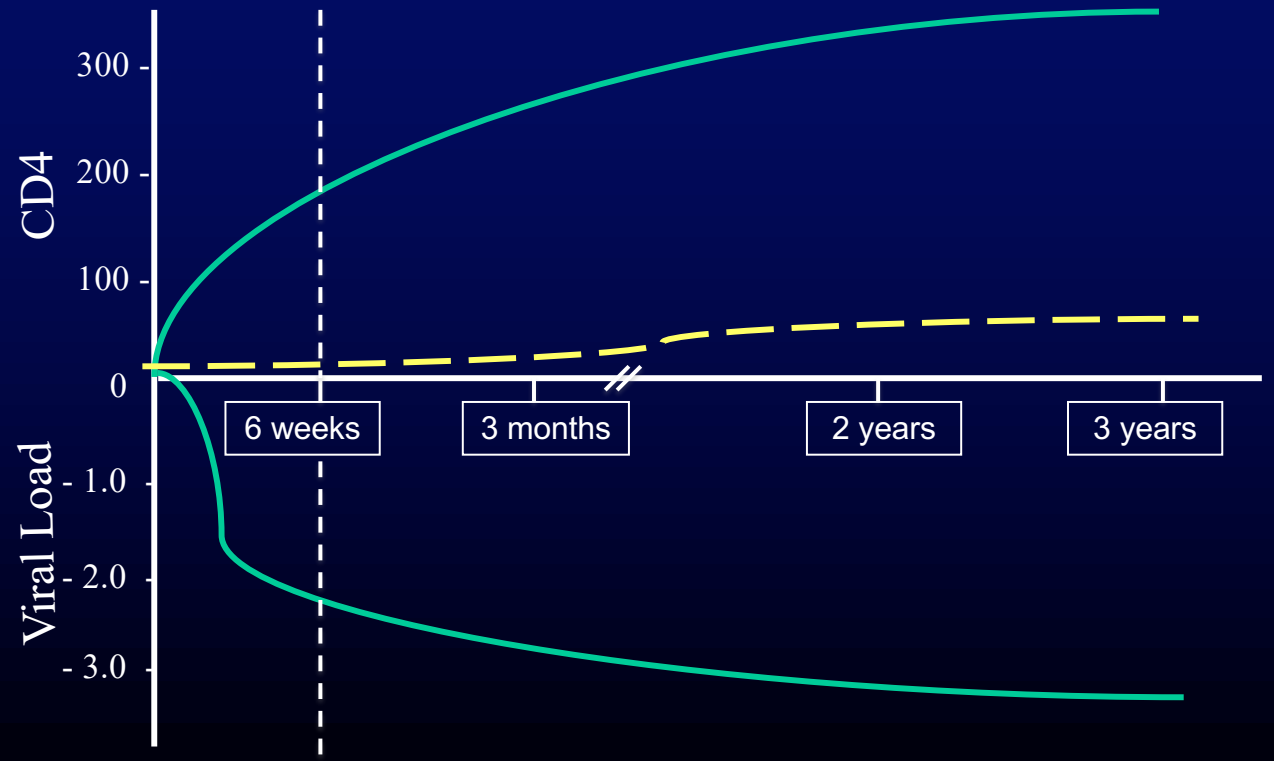
- 30 yo Female started on TDF / FTC /DRV / cobi 4 years ago
- **Initial:** HIV RNA 78,000 c/ml
  CD4 count 80 cells/ul
- **Now:** HIV RNA < 50 c/ml (persistently)
  CD4 167 cells/ul
- She is tolerating the regimen well

slido

Which regimen would you choose?

ⓘ Start presenting to display the poll results on this slide.

What is Immunologic Failure ?



Question

How do I manage an established PWH who has frequent STIs?

Case 9

- 35 yo MSM is followed by you
- Diagnosed 10 years ago with HIV infection
- **Current:** HIV RNA < 20 c/ml
  CD4 count 525 cells/ul
- On BIC/ TAF / FTC
- Has a history of recurrent STIs ~ every 6 – 12 weeks

(individually or in combination)

  - Syphilis
  - GC
  - Chlamydia

slido

What do you recommend at this point?

ⓘ Start presenting to display the poll results on this slide.

Conclusions

- ARV therapy should be initiated with an InSTI-based regimen (unless otherwise indicated), as close to time of Dx as possible
- Watch out for divalent cation intake in PWH taking InSTIs
- Weight gain is associated with initiation of ARV Rx, with more weight gain observed in InSTI- and TAF-containing regimens
- DTG is a drug of choice in pregnant women (GIVE FOLATE)
- Simplification of complex regimens is ‘do-able’
- Virologic “Blips” are not Virologic Failure, it’s biology!
- “Immunologic” Failure is not “Failure,” it’s biology (too)!
- Consider use of episodic doxycycline for individuals with frequent STI epsodes

Question-and-Answer Session

2022 Ryan White HIV/AIDS Program CLINICAL CONFERENCE