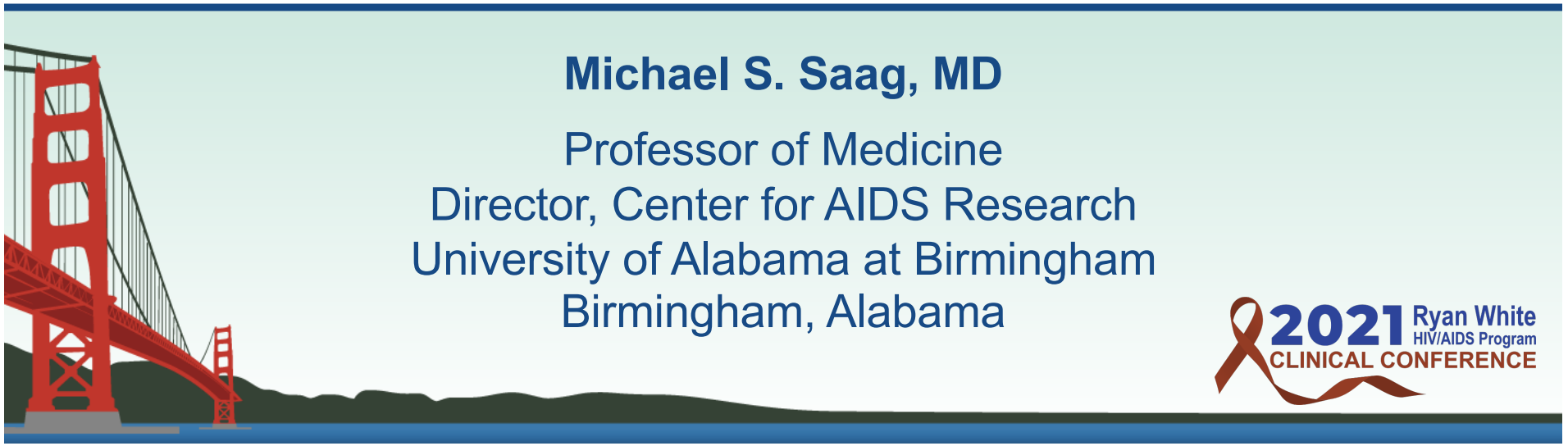
# Cases From the Clinic(ians):
# Antiretroviral Therapy Cases and Panel Discussion



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2021 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

# 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. (Updated 9/30/21)

# Learning Objectives

After attending this presentation, learners will be able to select antiretroviral therapy and/or manage patients who :

- Are starting initial therapy
- Are Elite Controllers
- Have InSTI-associated weight gain
- Have persistent low-level viremia
- Have a discordant CD4+ count response to ART
- Have ‘Blips’
- Are aging

# Question

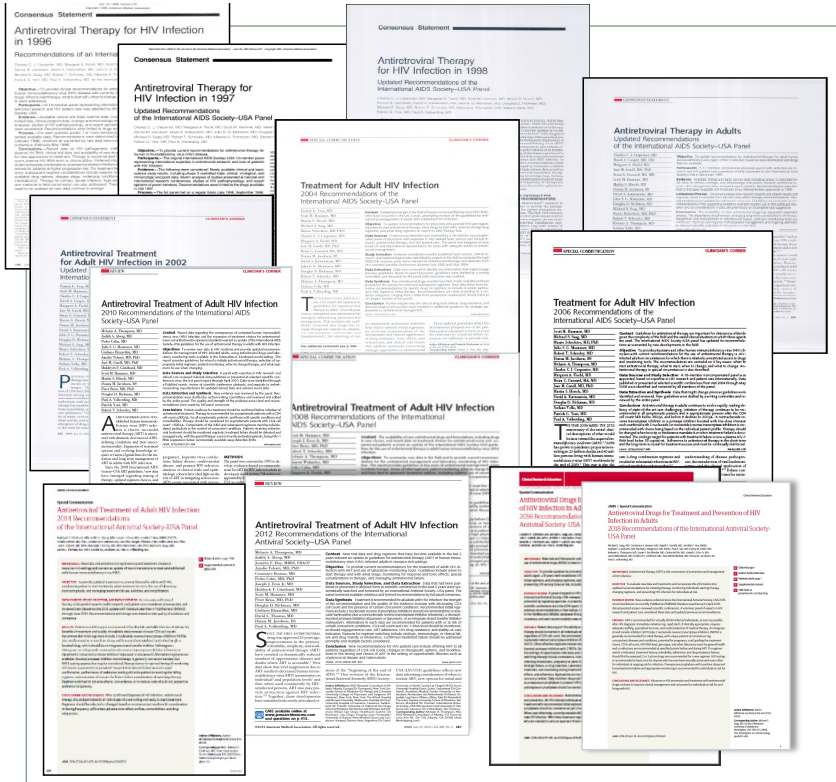
What initial regimen should I prescribe?

# 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
- HBV immune
- Ok to start therapy if you think he should

## ARS Question 1: What additional lab test should I order?

1. InSTI Genotype
2. Toxo Antibody
3. HLA-B*5701
4. Serum Cryptococcal Antigen
5. Urine Histo Antigen




Clinical Review & Education

JAMA | Special Communication

# Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults

## 2020 Recommendations of the International Antiviral Society–USA Panel

Michael S. Saag, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Melanie A. Thompson, MD; Paul E. Sax, MD; Davey M. Smith, MD; Constance A. Benson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

**IMPORTANCE** Data on the use of antiretroviral drugs, including new drugs and formulations, for the treatment and prevention of HIV infection continue to guide optimal practices.

**OBJECTIVE** To evaluate new data and incorporate them into current recommendations for initiating HIV therapy, monitoring individuals starting on therapy, changing regimens, preventing HIV infection for those at risk, and special considerations for older people with HIV.

**EVIDENCE REVIEW** New evidence was collected since the previous International Antiviral (formerly AIDS) Society–USA recommendations in 2018, including data published or presented at peer-reviewed scientific conferences through August 22, 2020. A volunteer panel of 15 experts in HIV research and patient care considered these data and updated previous recommendations.

**FINDINGS** From 5316 citations about antiretroviral drugs identified, 549 were included to form the evidence basis for these recommendations. Antiretroviral therapy is recommended as soon as possible for all individuals with HIV who have detectable viremia. Most patients can start with a 3-drug regimen or now a 2-drug regimen, which includes an integrase strand transfer inhibitor. Effective options are available for patients who may be pregnant, those who have specific clinical conditions, such as kidney, liver, or cardiovascular disease, those who have opportunistic diseases, or those who have health care access issues. Recommended for the first time, a long-acting antiretroviral regimen injected once every 4 weeks for treatment or every 8 weeks pending approval by regulatory bodies and availability. For individuals at risk for HIV, preexposure prophylaxis with an oral regimen is recommended or, pending approval by regulatory bodies and availability, with a long-acting injection given every 8 weeks. Monitoring before and during therapy for effectiveness and safety is recommended. Switching therapy for virological failure is relatively rare at this time, and the recommendations for switching therapies for convenience and for other reasons are included. With the survival benefits provided by therapy, recommendations are made for older individuals with HIV. The current coronavirus disease 2019 pandemic poses particular challenges for HIV research, care, and efforts to end the HIV epidemic.

**CONCLUSION AND RELEVANCE** Advances in HIV prevention and management with antiretroviral drugs continue to improve clinical care and outcomes among individuals at risk for and with HIV.

Supplemental content

CME Quiz at jamacmelookup.com

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JAMA. doi:10.1001/jama.2020.17025
Published online October 14, 2020.

# IAS–USA ARV Guidelines 1996 – 2020

https://jamanetwork.com/journals/jama/fullarticle/2771873

# Lab Continuum

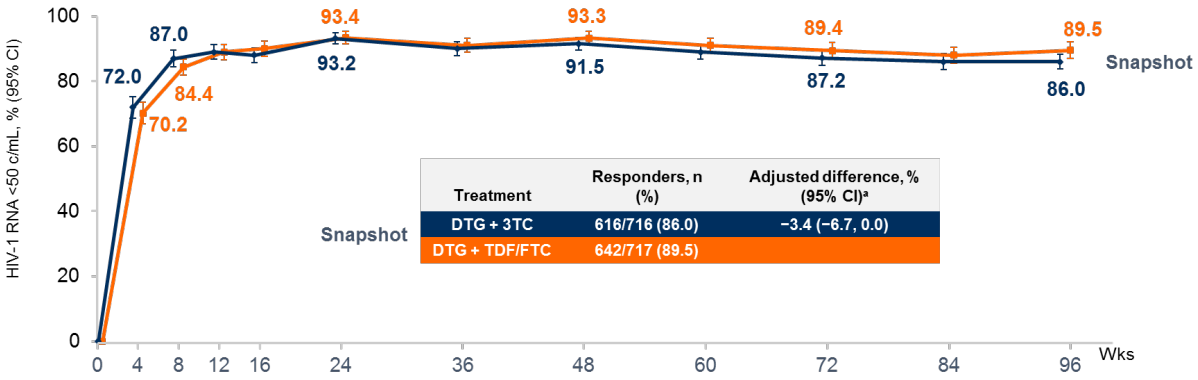
| Laboratory Test | HIV Negative | PrEP | PEP | At HIV Diagnosis | During ART | At Virologic Failure |
|---|---|---|---|---|---|---|
| Rapid HIV Antibody | + | Yes before PrEP | Before PEP | | | |
| Combination HIV Antigen/ Antibody | + | At time of PrEP but do not wait for results | Before and After PEP | | | |
| HIV RNA Test | For persons at higher risk | | | + | + | + |
| CD4 Cell Count | | | | + | Every 6 months until >250/µL for 1 year then stop. | + |
| HIV RT-PR Genotype | | | | + | | + |
| HIV Integrase Genotype Test | | | | Partner has a failing ART with InSTI | | If failing ART regimen with InSTI |
| Cryptococcal antigen test if CD4 cell count is <100/µL | | | | + | | |
| Safety labs, and coinfection screening (STI, viral hepatitis) | Per risks | + | + | + | + | + |

# ARS Question 2: Which regimen would you choose?

1. ABC/ 3TC / DTG (fdc)
2. TAF/ FTC (fdc) + DTG
3. TAF / FTC/ ELV / cobi (fdc)
4. TAF/ FTC / BIC (fdc)
5. 3TC/DTG (fdc)
6. TAF/ FTC /DRVcobi / fdc)
7. Some other option (e.g., DRV/r + DTG or …)

- 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

# DTG + 3TC Non-inferior to DTG + TDF/FTC: Snapshot VL <50 at Week 96




In small subset with CD4 count <200, virologic suppression rate was numerically lower in 2-drug group, but not related to virologic failure

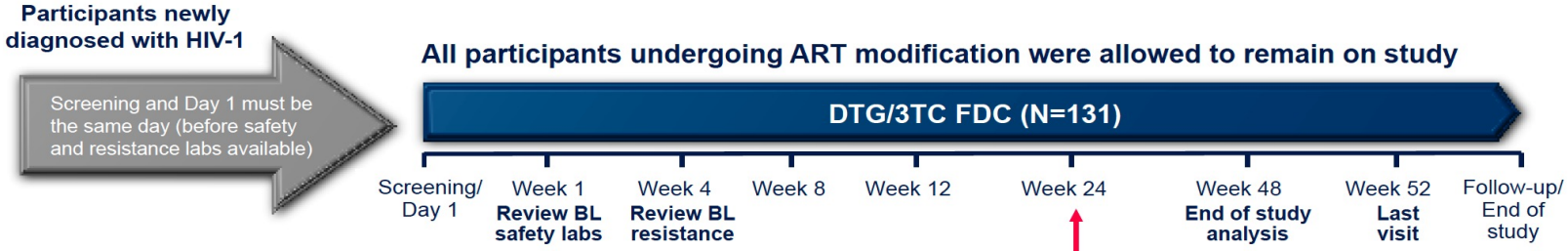
- No treatment emergent resistance (INSTI or NRTI) in either arm
- Blips not more frequent in 2-drug arm
- Proportion of viral load <40/target not-detected similar in 2- and 3-drug arms
- Similar results at week 144



Cahn. Lancet. 2019;393:143. Cahn. JAIDS. 2020;83:310. Cahn. HIV Glasgow 2020. Abstr P018

# STAT Is a Phase IIIb, Multicenter, Open-label, Single-Arm, Pilot Study Evaluating DTG/3TC as a Rapid Test-and-Treat Intervention

- In the primary analysis of STAT (ClinicalTrials.gov, NCT03945981) at Week 24, 78% (102/131) of all participants and 92% (102/111) of those with data available irrespective of ART achieved HIV-1 RNA <50 c/mL
- Here we show results from the key secondary efficacy analyses through Week 48 of the STAT study, including among participants with high baseline viral load (≥500,000 c/mL)




**Eligibility criteria**
- Adults ≥18 years of age
- ART naive
- Newly confirmed diagnosis of HIV-1 (within 14 days of initial diagnosis)

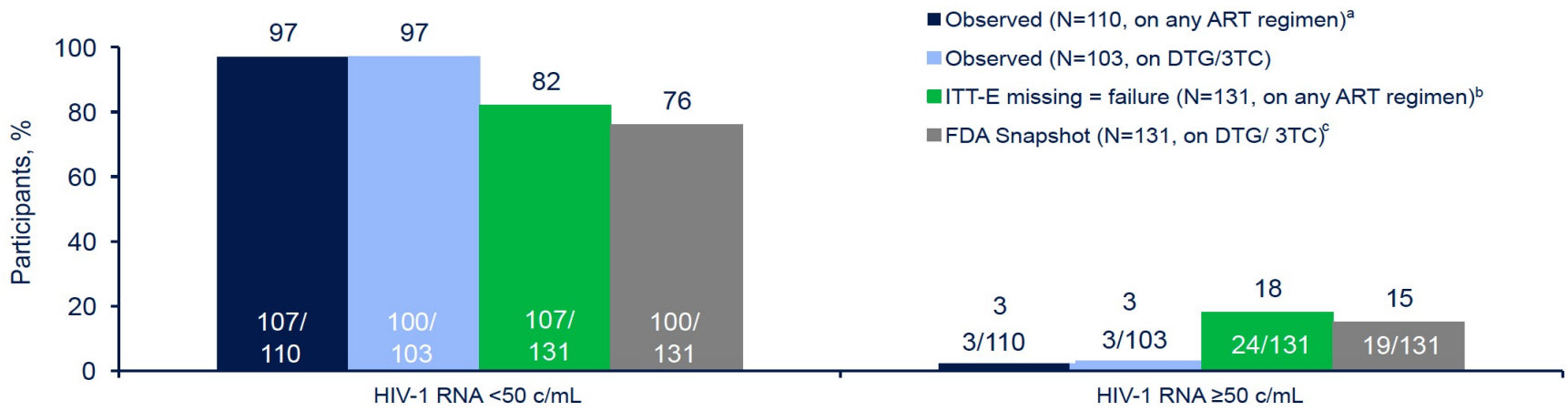
**Baseline criteria to switch from DTG/3TC**
- Creatinine clearance <30 mL/min/1.73 $m^2$
- Grade 3-4 lab abnormality
- Chronic HBV infection
- Transmitted resistance mutations (eg, M184V/I)

**Primary efficacy analysis**
**ITT-E missing = failure**
- HIV-1 RNA <50 c/mL (irrespective of treatment)
- HIV-1 RNA ≥50 c/mL
  - Includes missing data while on study or missing data due to study withdrawal

**Other key efficacy analyses**
- Observed analysis
- Snapshot analysis

Rolle et al. *AIDS*. 2021;35:1957-1965.

# High Rates of Virologic Suppression Were Observed Across All Efficacy Analyses at Week 48

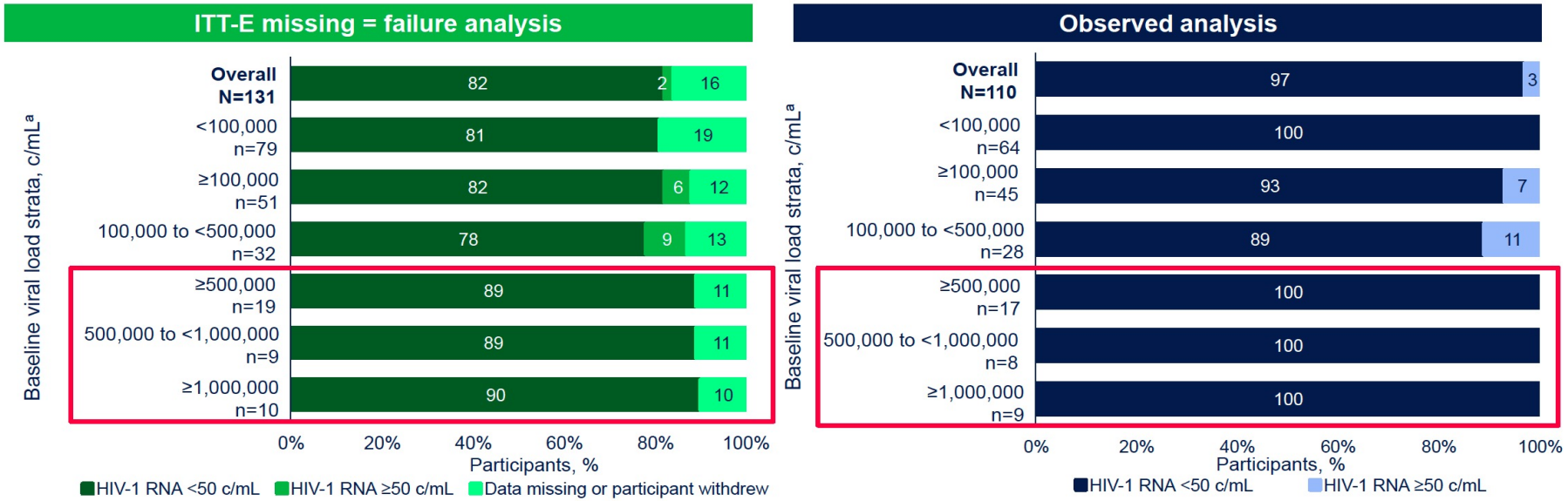



- ITT-E non-suppression rates were driven by non-virologic factors (ie, high withdrawal rate)
- Snapshot non-suppression rates were driven by study withdrawals and ART modifications

[a]The observed analysis included all participants with available HIV-1 RNA data, regardless of ART regimen. [b]The ITT-E missing = failure analysis included all participants in the ITT-E population, regardless of ART regimen. Of the 24 participants classified as HIV-1 RNA ≥50 c/mL, 3 had HIV-1 RNA ≥50 c/mL, 3 were on study but missing data at Week 48 (1 due to COVID-19), and 18 discontinued from study for non–treatment-related reasons (eg, withdrawn consent, lost to follow-up). [c]In the Snapshot analysis (missing data or switch considered failure), the 100 participants with HIV-1 RNA <50 c/mL were all on DTG/3TC; of the 19 participants classified as HIV-1 RNA ≥50 c/mL, 3 had HIV-1 RNA ≥50 c/mL (all under DTG/3TC), 10 modified ART, and 6 discontinued from study for non–treatment-related reasons (eg, withdrawn consent, lost to follow-up) and had HIV-1 RNA ≥50 c/mL; 12/131 had no virologic data at Week 48.

Rolle et al. IAS 2021; Virtual. Poster PEB182

# At Week 48, Virologic Suppression Rates Were High in Participants With Baseline Viral Load ≥500,000 c/mL




- 11/19 participants with baseline HIV-1 RNA ≥500,000 c/mL had CD4+ cell count <200 cells/mm$^3$; 10 achieved HIV-1 RNA <50 c/mL at Week 48 and 1 withdrew at Week 4 due to physician decision
- Median (95% CI) time to suppression for participants with baseline viral load ≥500,000 c/mL was 60 (56-169) days

ITT-E missing = failure analysis: all participants in the ITT-E population, regardless of ART regimen; observed analysis: all participants with available HIV-1 RNA data, regardless of ART regimen.
[a]1 (<1%) participant had missing plasma HIV-1 RNA results at baseline.

# Question

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

## ARS Question 3: Which regimen would you choose?

1. TAF/ FTC (fdc) + DTG
2. TAF/ FTC / BIC (fdc)
3. Cabotegravir + RPV IM every 8 weeks
4. Islatravir + Lenacapavir implant once yearly
5. bNAB + (Leronlimab or Albuvirtide) SQ QOW
6. 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

# 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; HLA-B57 neg
- Genotype determined from DNA is wild-type

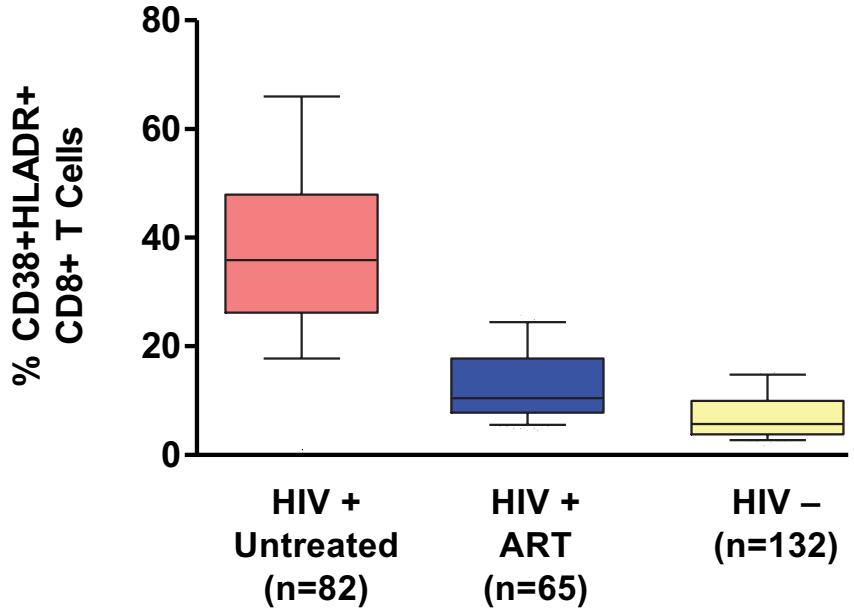
- No prior medical history.

- Ok to start therapy if you think he should

# ARS Question 4: Would you choose to start therapy at this time?

1. Yes
2. No
3. Maybe

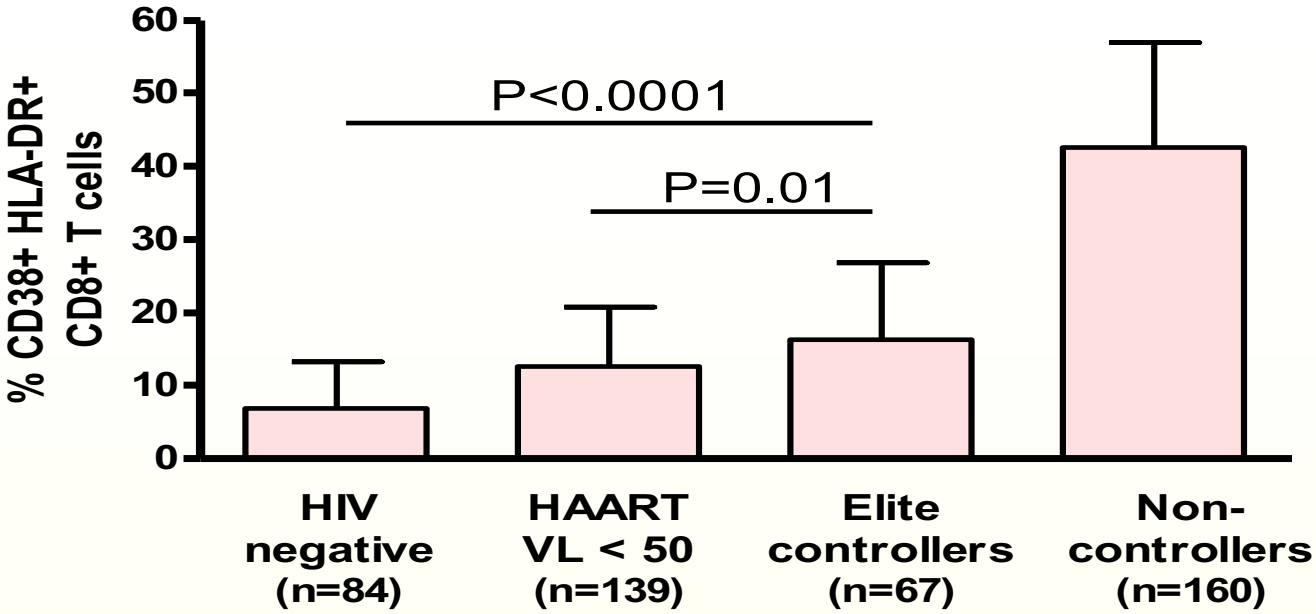
# T cell "activation" is lower in treated than untreated adults, but consistently higher than "normal"






*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 should ARV associated weight gain be managed?

# Case 3

- 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**

## ARS Question 5: At this point you would

1. **Keep her on her current Rx** (TAF/FTC/BIC)

   **Or Switch her to:**

2. TDF / FTC (fdc) + DTG
3. DTG / RLP (fdc)
4. TDF / FTC / DOR
5. TAF / FTC / DOR
6. TAF/ FTC / DRV/c (fdc)
7. Some other option

# Case 4

- 62 yo male started on ARV Rx years ago (resistance history: wild type virus) **returns to you for care after 4 years** (Rx'd elsewhere)
- Has been through several regimens; now on ABC/ 3TC / DTG (fdc)
- **Now:** HIV RNA < 20 c/ml (persistently)
  CD4 560 cells/ul
  Cholesterol 180 mg/dl (HDL 52 / LDL 100)
  Creat 1.3 / eCrCl = 80 cc/min
- Smoker
- PMHx negative (No cardiac history)
- On atorvastatin and daily low-dose ASA

# ARS Question 7: Besides asking him to quit smoking, what would you do?

1. Continue his current ARV Rx
2. Change his ABC/3TC to TAF / FTC containing Rx
3. Change his ABC/3TC to DRV/rit (continue DTG)
4. Some other option

# Question

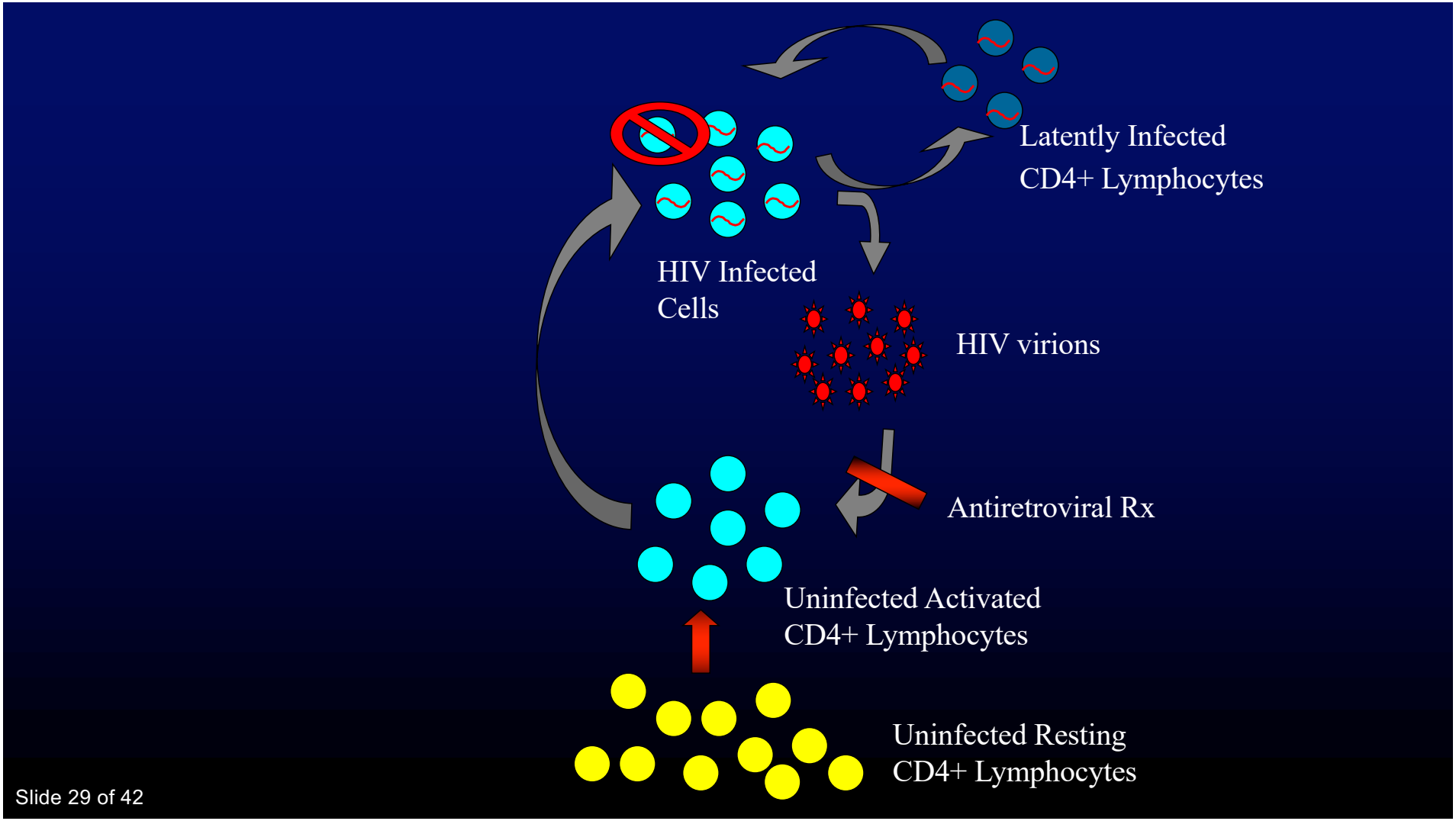
What do I do with a patient who has persistently detectable viremia?

# Case 5

- 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

# ARS Question 8: Should you change ARV therapy now?

1. Yes
2. No
3. Not sure


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

# Question

How do I manage ‘blips’?

# Case 6

- 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

## ARS Question 9: He claims full adherence. Which of the following is the most likely cause of the virologic failure?

1. Intermittent adherence to his regimen (despite his claims otherwise)
2. Occult recreational drug use
3. Recent Initiation of a Multi-vitamin
4. De novo emergence of viral resistance
5. Interference with lab results by a Russian Bot

# Question

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

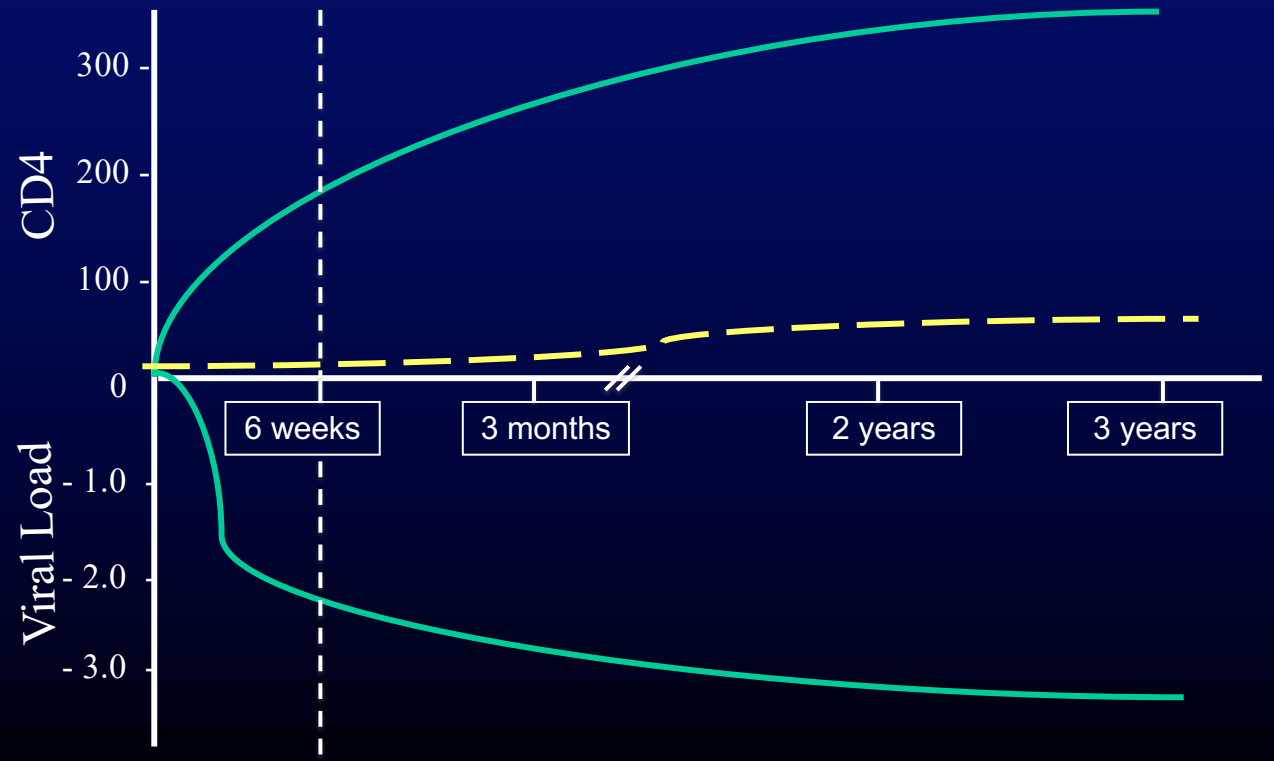
# Case 7

- 30 yo Female started on TDF / FTC /DRV / cobi  3 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

# ARS Question 10: Which regimen would you choose?

1. Continue her current Antiretroviral Rx
2. Change her ARV Rx to 2 nucs and an NNRTI
3. Change her ARV Rx to 2 nucs and a different boosted PI
4. Change her ARV Rx to 2 nucs and an STII (integrase inhibitor)
5. Change her ARV Rx to an STII and a different boosted PI
6. Something else

# What is Immunologic Failure ?



# Question

What is the best way to evaluate our patients as they age with HIV?

# Case 8

- 60 yo man was diagnosed with HIV infection 17 years ago
- Asymptomatic
- **Initial:** HIV RNA < 50 c/ml (HIV DNA positive)
  CD4 count 870 cells/ul

- Other labs are normal
- On fdc BIC / TAF / FTC

# ARS Question 11: How would you assess cognitive function?

1. Assessments should be conducted based on the patient's report of symptoms (memory changes or changes in other mental functions)
2. Routine assessments should be conducted annually
3. Routine assessments should be conducted every other year
4. Cognition can be assessed by a simple question: "How's your thinking?"
5. Some other answer

## ARS Question 12: How frequently are you performing frailty assessments in your clinical practice?

1. Not at all
2. Only when you suspect a patient may be frail
3. At regular intervals in older people with HIV (routine assessment)

# Conclusions

- ARV therapy should be initiated with an InSTI-based regimen (unless otherwise indicated), as close to time of Dx as possible
- Weight gain is associated with initiation of ARV Rx, although management of patients with weight gain is difficult
- Most Elite Controllers should be treated with ARV Rx
- Do not change Rx in setting of low-level viremia…BUT…Check for drug-drug interactions
- Incorporate Frailty and Cognition assessments into practice

# Question-and-Answer Session

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