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?

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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

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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

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IAS–USA
ARV Guidelines
1996 – 2020

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

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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	+	+	+	+	+

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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

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

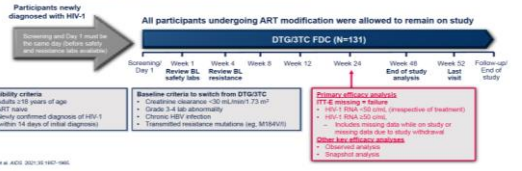
In small subset with CD4 count <200, virologic suppression rate was numerically lower in 2-drug group, but not related to virologic failure

- 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

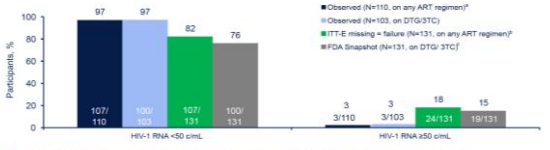
Cahn. Lancet. 2019;393:143. Cahn. JAIDS. 2020;83:310. Cahn. HIV Glasgow 2020. Abstr P018

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

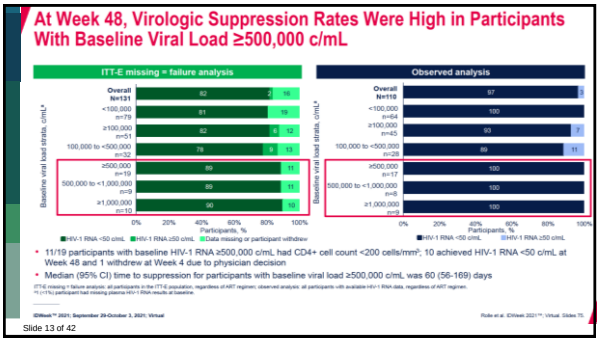
- In the primary analysis of STAT (ClinicalTrials.gov, NCT03945981) at Week 24, 78% (102/131) of all participants and 92% (102/111) of those with data available irrespective of ART achieved HIV-1 RNA <50 c/mL
- Here we show results from the key secondary efficacy analyses through Week 48 of the STAT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



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



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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**?

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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

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

1. Yes
2. No
3. Maybe

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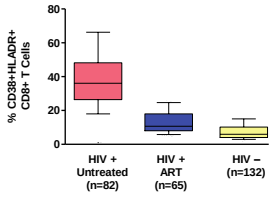
T cell "activation" is lower in treated than untreated adults, but consistently higher than "normal"



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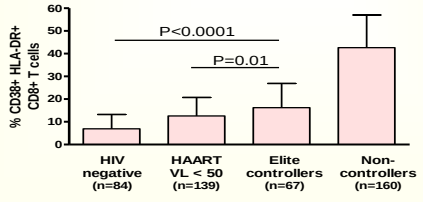
Hunt et al JID 2003, PLoS ONE 2011 and unpublished

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?

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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**

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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

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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

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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

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Question

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

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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

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ARS Question 8: Should you change ARV therapy now?

1. Yes
2. No
3. Not sure

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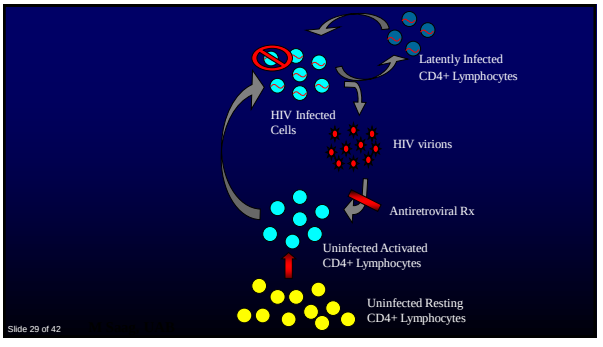

Question

How do I manage 'blips'?

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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

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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

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Question

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

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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

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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

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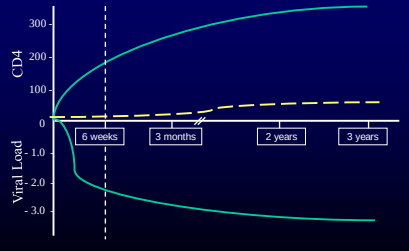
What is Immunologic Failure ?



Question

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

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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

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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

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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)

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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

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