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

Michael S. Saag, MD
Professor of Medicine
Associate Dean for Global Health
University of Alabama at Birmingham
Birmingham, Alabama

Financial Relationships With Commercial Entities

Dr Saag has received research grants and support awarded to his institution from Gilead Sciences, Inc and ViiV Healthcare. (Updated 4/30/21)

Slide 2 of 45

Learning Objectives

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

- Are starting initial therapy
- Have ARV-associated weight gain
- Are/ plan to become pregnant
- Are aging
- Have virologic failure

Slide 3 of 45

Question

What regimen should I use as initial therapy?

Slide 4 of 45

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

Slide 5 of 45

ARS Question 1: Which regimen would you choose?

1. TDF / 3TC / low dose (400mg) EFV (fdc; generic)
2. ABC/ 3TC / DTG (fdc)
3. TAF/ FTC (fdc) + DTG
4. TAF / FTC/ ELV / cobi (fdc)
5. TAF/ FTC / BIC (fdc)
6. 3TC/DTG (fdc)
7. Cabotegravir + RPV IM every 8 weeks
8. TAF/ FTC (fdc) + DRV/r (or cobi / fdc)
9. Some other option (e.g., DRV/r + DTG or …)

Slide 6 of 45

ARS Question 2: Which group of PWH is less likely to receive ARV therapy in a timely fashion?

1. Those living in the Southern US
2. Those living in the Western US
3. Blacks
4. Caucasians
5. IVDUs
6. Some other answer

Slide 7 of 45

Case 2

- 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

Slide 8 of 45

ARS Question 3: 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

Slide 9 of 45

Question

Should I simplify an initial regimen?

Slide 10 of 45

Case 3

- 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; HBV immune
- 4 months ago started on DTG + TAF/FTC; Doing well
  - HIV RNA < 20
  - CD4 Count 270 cells/ ul

Slide 11 of 45

ARS Question 4: Should the Regimen be Changed?

1. No. Don't change the regimen

Yes…Change the regimen to:

2. DTG + 3TC
3. Cabotegravir + RPV IM every 8 weeks
4. Some other choice

Slide 12 of 45

Question

How should ARV associated weight gain be managed?

Slide 13 of 45

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**

Slide 14 of 45

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

Slide 15 of 45

Question

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

Slide 16 of 45

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

Slide 17 of 45

ARS Question 6: At this point which regimen would you choose?

1. TDF / FTC / EFV (fdc)
2. ABC/ 3TC / DTG (fdc)
3. TAF / FTC/ ELV / cobi (fdc)
4. TDF / FTC / RPV (fdc)
5. TDF/ 3TC (fdc) / DTG (fdc)
6. TAF/ FTC (fdc) / DRV/r
7. 3TC / DTG
8. TDF / FTC / ATV/r
9. Some other option

Slide 18 of 45

IMPAACT 2010: Results through Delivery

- Virologic efficacy of DTG-based ART at delivery superior to that of EFV/FTC/TDF (97.5% vs. 91%, p=0.005)
- Time to viral suppression shorter with DTG-based ART (*P* < .001)
- Adverse pregnancy outcomes significantly less frequent with DTG + FTC/TAF (24.1%) vs DTG + FTC/TDF (32.9%) and EFV/FTC/TDF (32.7%)
- Neonatal death significantly less frequent with DTG + FTC/TAF vs EFV/FTC/TDF (P = .019)

ART Pregnancy Covid-1

Chinua. CROI 2020. Abstr 130LB. NCT03048422.

Question

Should I stop abacavir in older patients?

Slide 20 of 70

Case 7

- 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

Slide 21 of 70

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

Slide 22 of 70

ARS Question 8: Which factor places PWH at Highest Risk for MI?

1. ABC use
2. LDL Cholesterol level
3. Smoking
4. Hypertension
5. Family History
6. Bad Luck

Slide 23 of 70

Question

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

Slide 24 of 45

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; HLA-B*5701 neg
- On fdc BIC / TAF / FTC

Slide 25 of 45

ARS Question 9: 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

Slide 26 of 45

ARS Question 10: 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)

Slide 27 of 45

Question

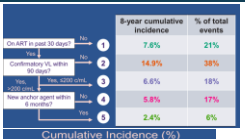
How do I manage virologic failure ?

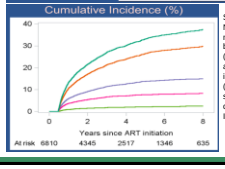
Slide 28 of 45

Characterizing First Virologic Failure: CNICS Analysis

- 6,810 1st Line patients
- Failure broadly defined – at least one VL > 200 post 24 wks
- 5 categories of VF
- 2,010 virologic failures – 21.5 % at 2 years and 37.4% at 8 years

Cisgender woman vs. man	1.30 (1.17, 1.46)
Black vs. White	1.45 (1.31, 1.62)
Hispanic vs. White	0.91 (0.79, 1.06)
Heterosexual vs. MSM	1.28 (1.15, 1.43)
IDU vs. MSM	1.80 (1.59, 2.03)
Age, per 10-year increase	0.97 (0.93, 1.01)
Calendar year	0.92 (0.91, 0.94)
NNRTI vs. INSTI	1.14 (1.01, 1.28)
PI vs. INSTI	1.83 (1.62, 2.07)
Other vs. INSTI	1.29 (1.09, 1.53)
CD4, per 100-cell/µL increase	0.90 (0.88, 0.92)





Starting on NNRTI 1.5x more likely to be in category 4 (confirmed VF) and 2.5x to be in category 5 (confirmed with switch) compared to INSTI

Slide 29 of 21 Davy-Mendez et al CROI 2021

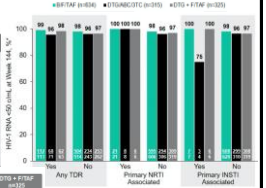
Impact of Baseline Resistance on INSTI-based Initial therapy

- Two large blinded treatment naïve studies comparing B/F/TAF with DTG/ABC/3TC or DTG plus F/TAF
- Baseline RT and PI sequencing and retrospective next gen sequencing for INSTI and NRTI resistance

Frequency of Preexisting Baseline Resistance Substitutions

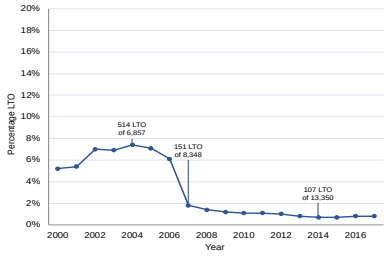
Participants With Resistance Substitutions at Baseline, n (%)	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325
Primary NRTI associated	21 (3)	8 (3)	6 (2)
1–2 TAMs	19 (3)	6 (2)	6 (2)
K65E/R	2 (<1)	1 (<1)	0
Primary INSTI associated	7 (1)	4 (1)	6 (2)
T97A	6 (<1)	4 (1)	6 (2)
Q148H	1 (<1)	0	0
Secondary INSTI associated	326 (52)	152 (48)	161 (50)
Primary NNRTI associated	92 (15)	53 (17)	45 (14)
K103N/S	42 (7)	27 (9)	23 (7)
E138A/G/K/Q	28 (4)	17 (5)	14 (4)
Primary PI associated	19 (3)	13 (4)	12 (4)

Participants, n, (%)	B/F/TAF n=634	DTG/ABC/3TC n=315	DTG + F/TAF n=325
Met criteria for resistance testing*	8 (1.3)	6 (1.9)	7 (2.2)
NRTI resistance detected	0	0	0
INSTI resistance detected	0	0	0



Slide 30 of 21

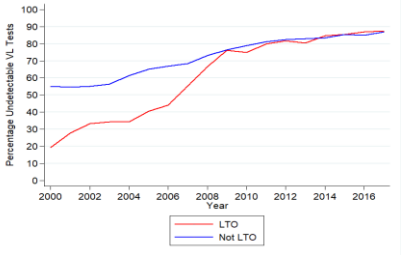
Prevalence of Patients with Limited Treatment Options



Slide 31 of 45

Bajema, et al, AIDS 2020

Virologic Success in Those with or without LTO



Slide 32 of 45

Bajema, et al, AIDS 2020

Discussion

- Confirm the virologic failure
- Explore all prior regimens and resistance tests
- Identify 2 fully active drugs (if possible)
  - Use dolutegravir (50 mg) twice daily
  - Some form of tenofovir (as long as no K65R)
  - Boosted darunavir
  - 3TC or FTC (despite resistance)
    - Ibalizumab
    - **Fostemsavir**

Slide 33 of 45

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)
- Incorporate Frailty and Cognition assessments into practice
- Use two active drugs (if possible) in treating Virologic Failure

Slide 34 of 45

Question-and-Answer Session