Treating HIV in 2019: Interactive Cases From the Clinic(ians) and Panel Discussion

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Panelists
- Rajesh Gandhi, MD
- Michelle Iandiorio, MD
- Jesse Moore, MD
- Paula Seal, MD
- Phillip Bolduc, MD
- Steven Johnson, MD

Financial Relationships With Commercial Entities
Dr Saag has received research grants and support awarded to his institution from Gilead Sciences, Inc, and ViV Healthcare. (Updated 11/21/19)
Learning Objectives

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

- Are starting initial therapy
- Are Elite Controllers
- Are debating between starting TDF or TAF
- Have persistent low level viremia
- Have End-Stage Renal Disease
- Have a slow CD4 count response to ART

Question

Seems like we are now starting ARV therapy for about everyone, what about starting therapy immediately at time of diagnosis?

Case 1

- 30 yo Male was diagnosed with HIV infection 4 hours ago in the ER
- Asymptomatic
- Initial: No Viral Load, CD4, Resistance Data, or HLA-B57 neg
- Other labs are normal
  - WBC 3800 / Lymphocytes 20%
- No prior medical history.
- Ok to start therapy if you think he should
**ARS Question 1: When would you choose to start therapy?**

A. Right now in the ED  
B. Within 1 or 2 days (outpatient Clinic)  
C. In the next 2 weeks (outpatient Clinic)  
D. Within 2 to 4 weeks  
E. Some other option

**Question**

What regimen should I use as initial therapy for this patient?

**ARS Question 2: At this point, which regimen would you choose?**

A. TDF / 3TC / low dose (400mg) EFV (fdc; generic)  
B. ABC / 3TC / DTG (fdc)  
C. TAF / FTC (fdc) + DTG  
D. DTG + 3TC  
E. TAF / FTC / ELV / cobi (fdc)  
F. TAF / FTC / BIC (fdc)  
G. TAF / FTC (fdc) + RAL (once daily)  
H. TAF / FTC / RPV (fdc)  
I. TAF / FTC (fdc) + DRV/r (or cobi / fdc)  
J. Some other option (e.g., DRV/r + DTG or …)
**Question**

What regimen should I use as initial therapy?

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**Case 2**

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial:** HIV RNA 28,000 c/ml
  - CD4 count 650 cells/ul
- Other labs are normal; **HLA-B57 positive**
- Genotype is Wild-type virus
- No prior medical history. Normal renal function
- Ok to start therapy if you think he should

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**ARS Question 3:** At this point, which regimen would you choose?

- A. TDF / 3TC / low dose (400mg) EFV (fdc; generic)
- B. ABC / 3TC / DTG (fdc)
- C. TAF / FTC (fdc) + DTG
- D. TAF / FTC / ELV / cobi (fdc)
- E. TAF / FTC / BIC (fdc)
- F. TAF / FTC (fdc) + RAL (once daily)
- G. TAF / FTC / RPV (fdc)
- H. TAF / FTC (fdc) + DRV/r (or cobi / fdc)
- I. Some other option (e.g., DRV/r + DTG or …)
ARS Question 4: Would you use DTG / 3TC as initial therapy?

A. Yes  
B. No  
C. Not sure

GEMINI: Initial ART with DTG/3TC

DTG + 3TC IS NON-INFERIOR TO DTG + TDF/FTC IN SNAPSHOT HIV-1 RNA <50 c/mL AT WEEK 96

Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 48 (Snapshot Analysis) by Baseline Plasma HIV-1 RNA

- Eron et al. HIV DART and Emerging Viruses 2018; Miami, FL. Slides 7.

Cahn et al. #WEAB0404LB
Recommended Initial Regimens: InSTI Plus 2 nRTIs

- Bictegravir/TAF/emtricitabine
- Dolutegravir/abacavir/lamivudine
- Dolutegravir plus (TAF/emtricitabine)

ARS Question 5: Would you use TAF or TDF with an InSTI?

A. TAF
B. TDF
C. Either
Renal Toxicity


Bone Toxicity

Question

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

Case 3

- 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 6: Would you choose to start therapy at this time?

A. Yes
B. No
C. Maybe
"T cell "activation" is lower in treated than untreated adults, but consistently higher than "normal"


<table>
<thead>
<tr>
<th>% CD38+HLADR+CD8+ T Cells</th>
<th>HIV+</th>
<th>HIV+ ART</th>
<th>HIV-</th>
<th>HIV- ART</th>
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</thead>
<tbody>
<tr>
<td>HIV Negative (n=82)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Non-Controller (n=65)</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>HAART (n=132)</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

P < 0.001

Question

Should I change a regimen when low level detectable virus is present?

Case 4

- 55 yo male referred to you for evaluation
- Diagnosed 18 years ago with HIV infection
- Initial: HIV RNA 936,000c/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 / TDF/FTC
  - EFV/ FTC / TDF (ld)
  - Now DTG / DRV/c / 3TC
- No historical resistance tests are available
ARS Question 7: Should you change ARV therapy now?

A. Yes
B. No
C. Not sure

Virologic Failure, Low Level Viremia, and Blips

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>≤6 months</th>
<th>&gt;6 to 12 months</th>
<th>&gt;12 months</th>
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</thead>
<tbody>
<tr>
<td>Pre-ART viral load median</td>
<td>28000</td>
<td>62457</td>
<td>62713</td>
</tr>
<tr>
<td>Year of ART initiation median</td>
<td>2011</td>
<td>2011</td>
<td>2011</td>
</tr>
<tr>
<td>ART anchor drug(s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI</td>
<td>40%</td>
<td>50%</td>
<td>46%</td>
</tr>
<tr>
<td>PI</td>
<td>32%</td>
<td>36%</td>
<td>45%</td>
</tr>
<tr>
<td>INI</td>
<td>31%</td>
<td>16%</td>
<td>13%</td>
</tr>
<tr>
<td>CD4 count, cells/µL median</td>
<td>440</td>
<td>460</td>
<td>460</td>
</tr>
<tr>
<td>AIDS diagnosis</td>
<td>12%</td>
<td>14%</td>
<td>20%</td>
</tr>
<tr>
<td>Hepatitis B co-infection</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Hepatitis C co-infection</td>
<td>10%</td>
<td>9%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Virologic Failure, Low Level Viremia, and Blips

- Virolologic failure
- Low-level viremia
- Viral blip

Time since art suppression, years

≥12 months
≥6 to 12 months
≤6 months
Question

Does InSTI therapy cause weight gain?

Case 4

> 47 year old woman starts on BIC/FTC/TAF 12 months ago from her original ARV regimen (TDF/FTC/DRV/r)
> Diagnosed 4 years ago
> • Initial: HIV RNA 28,000 c/ml (Wildtype 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

Case 5

ARS Question 8: At this point you would

A. Keep her on her current Rx (TAF/FTC/BIC)
   or Switch her to:
   B. TDF/ FTC (fdc) / DRV/r
   C. TAF/ FTC / DRV/c (fdc)
   D. TDF / FTC / RPV (fdc)
   E. DTG / RLP (fdc)
   F. TAF / FTC / ATV/c
   G. Some other option
Long-term weight gain (mean 2.0 years)

Weight gain after ~2 years, comparing ART regimens in adjusted analyses

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Years on regimen</th>
<th>βWeight gain (kg)</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFV (ref)</td>
<td>427</td>
<td>0.38</td>
<td>0.20, 0.66</td>
<td>0.01</td>
</tr>
<tr>
<td>RPV</td>
<td>349</td>
<td>0.08</td>
<td>-0.33, 0.50</td>
<td>0.67</td>
</tr>
<tr>
<td>ATV</td>
<td>96</td>
<td>0.62</td>
<td>0.20, 1.24</td>
<td>0.04</td>
</tr>
<tr>
<td>DRV</td>
<td>264</td>
<td>1.07</td>
<td>0.53, 1.61</td>
<td>0.00</td>
</tr>
<tr>
<td>RAL</td>
<td>99</td>
<td>0.55</td>
<td>0.32, 0.78</td>
<td>0.01</td>
</tr>
<tr>
<td>EVG/TDF</td>
<td>796</td>
<td>0.14</td>
<td>-0.05, 0.33</td>
<td>0.18</td>
</tr>
<tr>
<td>DTG/TDF</td>
<td>225</td>
<td>-0.05</td>
<td>-0.32, 0.22</td>
<td>0.76</td>
</tr>
</tbody>
</table>
| DTG/ABC               | 383              | 0.75              | 0.57, 1.14      | 0.00    

Note: All results were adjusted for baseline weight and duration of follow-up. *TAF regimens not included due to shorter mean follow-up time.

*DTG/TDF tested different vs EFV, RPV

**DTG/ABC tested different vs EFV, RPV, EVG/TDF

Change in Weight Overtime – NA-ACCORD
Bourgi et al CROI 2019

INSTI distribution: 4.74% Total: 1,887 (56%) HIV 2,138 (63%) EVG 654 (21%) TDF.
GAM plot: change in weight in kg over time

ADVANCE: Weight Gain

Cabotegravir vs Placebo for PrEP

Primary Outcome: Changes in weight

CAB vs. PBO

Venter IAS 2019 #WEAB0405LB
Morehouse IAS 2019 #WEAB0401DLB

Landovitz, et al, Abst 34 LB, CROI 2019
Question

Do I change ARV regimen in a patient with a discordant CD4 count response?

Case 6

- 48 yo man presents with newly diagnosed HIV infection
- Asymptomatic except for weight loss / fatigue
- Initial: HIV RNA 860,000 c/ml
  CD4 count 24 cells/ul
- Started on ARV Rx
- One year later his HIV RNA < 20 c/ml but his CD4 is 65 cells/ul
ARS Question 9: Should you change ARV therapy now?

A. Yes
B. No
C. Not sure

What is Immunologic Failure?

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 (ddc),
  - Now DTG / DRV/c / 3TC
- No historical resistance tests are available

ARS Question 10: Should you change ARV therapy now?

A. Yes
B. No
C. Not sure

Virologic Responses on Antiretroviral Therapy

Virologic Suppression

Virologic Blip


After virologic suppression, an isolated detectable HIV RNA level followed by return to virologic suppression.

HIV RNA (copies/mL)

Weeks

Antiretroviral Therapy Started

Latently Infected CD4+ Lymphocytes

HIV Infected Cells

HIV virions

Antiretroviral Rx

Uninfected Activated CD4+ Lymphocytes

Uninfected Resting CD4+ Lymphocytes

Virologic Failure

Question

What regimen should I use (or not use) in a patient with End-Stage Kidney Disease?

Case 8

- 57 year old man is referred to you for care; newly diagnosed with HIV
- Diagnosed when he presented for care at a local FQHC after years of not seeing a provider
- Initial Labs:
  - HIV RNA 147,000
  - CD4 Count 370 cells / ul
  - Serum creatinine 5.6 mg/dl
  - Estimated CrCl < 30 cc/min
  - Wild type virus
  - HLA B5701 negative

ARS Question 11: At this point which regimen would you choose?

A. DOR + TAF + 3TC (renally adjusted)
B. ABC/ 3TC / DTG (fdc)
C. TAF/ FTC / BIC (fdc)
D. TAF/ FTC (fdc) + DTG
E. DTG + abacavir + 3TC (renally adjusted)
F. DTG + 3TC (renally adjusted)
G. RAL (once daily) + abacavir + 3TC (renally adjusted)
H. DTG + rilpivirine
I. DTG + DRV/r (or cobi / fdc)
J. Some other option (e.g., DRV/r + DTG or …)
At this point which regimen would you choose?

A. DOR + TAF + 3TC (renally adjusted)
B. ABC/3TC/DTG (fdc)
C. TAF/FTC/BIC (fdc)
D. TAF/FTC (fdc) + DTG
E. DTG + abacavir + 3TC (renally adjusted)
F. DTG + 3TC (renally adjusted)
G. RAL (once daily) + abacavir + 3TC (renally adjusted)
H. DTG + rilpivirine
I. DTG + DRV/r (or cobi / fdc)
J. Some other option (e.g., DRV/r + DTG or ...)

Summary of ARVs in ESRD

<table>
<thead>
<tr>
<th>No Dose Adjustment</th>
<th>Dose Adjustment Required</th>
<th>Do Not Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>3TC</td>
<td>MOST FDCs</td>
</tr>
<tr>
<td>TAF (on hemodialysis)</td>
<td>FTC</td>
<td>- ELV (fdc)</td>
</tr>
<tr>
<td>EFV</td>
<td>(TDF)</td>
<td>- BIC (fdc)</td>
</tr>
<tr>
<td>DOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPV / ETV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV / r or ATZ / r</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Question

What regimen should I start when a patient returns after a long absence?
Case 9

- 55 yo male returns after being “Lost to Follow Up” for 2 years
- Diagnosed 7 years ago with HIV infection
- Initial Rx: TDF / FTC / RPV (Tolerated well)
- Initial: HIV RNA 86,000 c/ml (wildtype virus)
  CD4 count 70 cells/ul
- Status at last visit (2 years ago):
  HIV RNA 26 c/ml / CD4 count 325 cells/ul
- Now returns and wants to re-engage in care
- Lab results pending

ARS Question 12: What ARV therapy should you use now?

A. Same regimen as originally on
B. Start an InSTI-based regimen
C. Start a PI-based regimen
D. Wait for repeat resistance test, then choose regimen based on results
E. Some other answer

Question

How do I manage a heavily experienced patient who is experiencing virologic failure?
Prevalence of Patients with Limited Treatment Options

Virologic Success in Those with or without LTO

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
  - Compassionate Use Drug
### Conclusions

- ARV therapy should be initiated with an InSTI-based regimen (unless otherwise indicated), as close to time of Dx as possible
- Do not change Rx in setting of low-level viremia
- Do not change Rx in setting of low CD4 count response
- Avoid Fixed Dose Combination Therapy in patients with ESRD
- Weight gain is associated with initiation of ARV Rx, with more weight gain observed in InSTI regimens
- As a rule, restart the last successful regimen for those who were lost to care and now return

### Question-and-Answer Period