Dilemmas in HIV Management: A Case Based Discussion

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Panelists

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Case 1

- 40-year-old male presents with newly diagnosed HIV
- Asymptomatic
- Labs: CD4: 500 cells/ul
  HIV RNA: 25,000 copies/ml
- All other labs are normal
- HLA-B5701: negative
- Genotype: wildtype
- No additional medical history and he takes no medication
- He is ready to start treatment
ARS Question 1: Would you order a genotype that included integrase?

1. Yes
2. No
3. Not sure

Transmitted Drug Resistance

McClung RP, et al. CROI 2019 #3337
ARS Question 2: Which regimen would you start?

1. TDF / 3TC / low dose (400mg) EFV (generic)
2. ABC / 3TC / DTG
3. TAF / FTC + DTG
4. TAF / FTC / ELV / cobi
5. TAF / FTC / BIC
6. TAF / FTC + RAL (once daily)
7. TAF / FTC / RPV
8. TAF / FTC / DRV / cobi
9. Something else

Case 1

- Pt returns 4 weeks after starting treatment with TAF/FTC/Bictegravir
- CD4 count 580 and HIV RNA is < 20 copies/mL
- He remains undetectable over the next year
- He meets a female and they start dating and they want to have a child
- He comes to your for a consultation with his new girlfriend
- He asks about having condomless sex
ARS Question 3: Can they have condomless sex?

1. Yes
2. No
3. Not sure

Undetectable = Untransmittable

U=U refers to the concept that an individual with an undetectable HIV VL is incapable of transmitting their HIV infection to sexual partners. Reduced VL also significantly reduces risk of transmission via other routes:

- Unborn babies
- Healthcare workers who experience sharps/mucosal injuries

Undetectable VL in this context: <200 c/mL

Case 2: History

• This is a 53 year old male with PMH of HIV transferred from a provider in Washington DC—relocated due to his husband’s job
• He is on DTG and FTC/TDF
• CD4 count 464/42% and HIV viral load undetectable
• Serum creatinine 1.2-1.4 (CR clearances are always above 50)
• Unable to get TAF based regimen due to insurance

Case 2: History

• Insurance changes
• I discussed a change to TAF/FTC/BIC—he declined
• FTC/TDF changed to FTC/TAF and maintain DTG
• His plan was to finish out his remaining TDF and return in about 6 weeks for labs after the switch
• Missed his 6 week follow up for labs
• Comes back about 3 months later
History

• Comes back in and he has labs done
  – HIV viral load **3500** copies/ml
  – Admits to no missed doses
  – You review his medication history and he is only taking FTC/TAF (thought it was a new single tablet regimen with all components)-he forgot he did not want a change but knew I spoke to him about it
  – He was only on FTC/TDF/Efavirenz in the past with a change due to side effects

• Questions:
  – What are your next steps?

ARS Question 4: Would you add back his DTG right now?

1. Yes
2. No
3. Not sure
ARS Question 5: Would you check a genotype prior to the change?

1. Yes
2. No

Questions

• What resistance mutations do you expect?
• What regimen do you keep him on while waiting for a genotype?
Now what would you do and how do these mutations impact his regimen or a new regimen?

**M184I/V Mutation**

- Selected by Lamivudine (3TC) and Emtricitabine (FTC)
- M184I usually emerges before M184V because it results from a more common HIV-1 nucleotide substitution (G→A)
- Causes high level resistance to both drugs
- Selected quickly in the setting of non-suppressive therapy
- Referred to as a “good mutation” because of its effect on fitness and because it increases susceptibility to some NRTIs (when its alone it can cause hypersusceptibility to Zidovudine, Stavudine, and Tenofovir.
- It also causes low level resistance to Abacavir and Didanosine
K65R

- Selected by TDF, abacavir, stavudine, zalcitabine, and didanosine
- No cross resistance to Zidovudine (hypersusceptible)
- Low level resistance to TDF and NRTIs
Susceptibility to NRTIs for a Panel of K65R Viruses

PhenoSense Results for K65R alone (n=50)

- For tenofovir, all viruses were above the 4.0-fold cutoff for no response

Miller MD. AIDS Reviews, 2004; 6:22-33

Susceptibility to NRTIs for a Panel of K65R+M184V Viruses

PhenoSense Results for K65R + M184V (n=58)

Miller MD. AIDS Reviews, 2004; 6:22-33
Follow up

- He was placed on DCF-TAF and Dolutegravir while a genotype was drawn and pending
- 4 weeks later HIV viral load < 20 copies/m
- 3 months later HIV viral load <20 copies/mL
- 9 months later HIV viral load < 20 copies/mL

- Lessons learned:
  - Follow up call after making a switch

Case 3

- 34-year-old male presents with fever, headache, dry cough, 20 pound weight loss, progressive DOE over the last 3 weeks.
- Never tested for HIV
- No past medical history
- He works as a travel agent.
- No Etoh/IDU/crack use
- Sexually active with men
- History of Gonococcal urethritis 6 years ago (treated)
Case 3, continued

Exam

- T-101 F HR-92 BP-120/70 RR-22
- HEENT – oral thrush
- Neck – supple, No cervical lymphadenopathy
- Lungs – few crackles at bases bilaterally
- Heart –S1S2 no murmur, rubs, gallops
- Abdominal – soft, non-tender, no hepatosplenomegaly
- Extremities – no clubbing, cyanosis, edema
- Neuro – non-focal

Lab Studies

- Pulse oximetry – 95% (2 liters of oxygen)
- ABG: 7.45/36/68 95%
- CBC: wbc 3.2 H/H 12.9/37 plt 150K
- Electrolytes: normal; creatinine 1.2
- CXR: see next slide
Case 3

- 4th generation HIV test Positive Ag/AB
  - Reactive on multispot for HIV-1
- CD4 count- 30 cells/mm³
- Viral Load-250,000 copies/ml
- Bronchoscopy performed and the silver stain is positive for PCP
- He is started on TMP/SMX and corticosteroids
ARS question 6: While on rounds, the resident ask you if you should start antiretroviral therapy on this patient?

A. Treat the OI first and start HAART within 2 weeks.
B. Defer HAART until the patient has been established in the office.
C. Call Dr. for a phone consult.
D. Not sure.

Immediate vs. deferred ART in the setting of Acute OI: ACTG 5164

• Randomized Phase IV strategy trial in US, South Africa
• Determine the optimal timing of ART in the setting of an acute OI or serious bacterial illness
• Comparison of immediate (2 weeks) vs. delayed (45 days) ART
• Included confirmed or probable diagnoses of OIs and bacterial infections for which antimicrobial therapy are available

ACTG 5164: Immediate vs. Delayed ART with an Acute OI

- 228 pts with a treatable OI
  - Most common OI: PCP (63%)
  - TB excluded
  - Small number cryptococcal meningitis, Toxoplasmosis
- AIDS progression/death: immediate rx (14%) vs. delayed rx (24%)
- No difference in safety/toxicity, IRIS, or week 48 responses


When to Start ART in Patient with OI

<table>
<thead>
<tr>
<th>OI</th>
<th>When to start</th>
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<tbody>
<tr>
<td>Cryptosporidiosis, microsporidiosis, PML</td>
<td>As part of initial therapy of OI</td>
</tr>
<tr>
<td>PCP, MAC, Toxoplasma, most other OIs</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>If CD4 &lt;50: within 2 wk</td>
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<tr>
<td></td>
<td>If CD4 &gt;50: within 8-12 wks (TB meningitis: close</td>
</tr>
<tr>
<td></td>
<td>monitoring/consultation)</td>
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<tr>
<td>Cryptococcal meningitis</td>
<td>4-5 wks after anti-fungal Rx</td>
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When patient presents with OI or low CD4 count, ART should be started in hospital or soon after discharge

Case

- You order a genotype
- You start the patient on FTC/TAF and DTG while the patient is in the hospital
- He returns to your office 1 week after discharge and is feeling much better

Thank you