39 – Antiretroviral Therapy for Special Populations

Speaker: Roy Gulick, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 17-21, 2024

Antiretroviral Therapy (ART) for Special Populations

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- **Disclosures of Financial Relationships with Relevant Commercial Interests**

  - None

Special Populations

- acute/recent HIV infection
- acute opportunistic infection
- tuberculosis
- HIV-HBV co-infection
- HIV-HCV co-infection
- pregnancy
- post-HIV exposure (PEP)
  - occupational
  - non-occupational
- pre-HIV exposure (PrEP)

Question #1

PREVIEW QUESTION

A 22-year-old man presents with fever, mouth pain, and skin rash. PE reveals 3 small oral ulcers and diffuse macular rash. Labs show WBC 3K, platelets 89K, monospot negative, RPR NR, HIV antibody negative, HIV RNA 1,876,000 cps/ml.

Which statement is correct?

A. ART should not be offered.
B. ART would decrease his symptoms.
C. ART has long-term virologic benefits in this setting.
D. ART has long-term clinical benefits in this setting.

Acute or Recent HIV

- ART is RECOMMENDED.
- ART reduces symptoms and signs and reduces transmission.
- No long-term virologic, immunologic, or clinical data available.
- Goal is full virologic suppression.
- Obtain genotype prior to ART.
- If ART is started prior to genotype results, use **bictegravir, dolutegravir,** or **boosted darunavir,** together with tenofovir (TAF or TDF) + emtricitabine.
- If patient was on IM cabotegravir for PrEP, use **boosted darunavir-based** regimen (rather than integrase inhibitor-based).
- Can modify regimen, if needed, when genotype results return.

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Question #2

PREVIEW QUESTION

A 52-year-old woman is admitted for progressive SOB, is intubated, undergoes BAL and is found to have PCP. HIV Ab test is positive, CD4 103, HIV RNA 135,000 copies/ml. She is day 4 of IV trimethoprim-sulfa and corticosteroids and still intubated.

When should she start ART?

A. Immediately
B. In the next 2 weeks
C. After completing 21 days of trimethoprim-sulfa
D. At her first outpatient clinic visit

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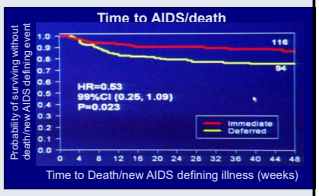
ACTG 5164: Immediate vs Delayed ART with an Acute OI

- 282 patients with treatable OI diagnosed within 14 days randomized to start ART within 48 hours vs. after 4 weeks
  - most common OI: PCP (63%)
- AIDS progression/death: immediate rx (14%) vs delayed rx (24%)
- No differences in safety/toxicity, IRIS, or week 48 responses
- Caution with CNS OI (e.g. cryptococcus, TB)



Zolopa PLoS One 2009;4:e5575

HIV-TB Co-infection

- Treat active TB the same with or without HIV.
- All PWH with TB should start TB meds immediately.
- In PWH with TB, timing of starting ART depends on CD4 count:
  - For CD4 <50, start ART ASAP, within 2 weeks of TB rx
  - For CD4 ≥50, start ART within 8 weeks of TB rx
- Start pregnant women with HIV and TB on ART as early as feasible.
- For TB meningitis, monitor closely.

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Question #3

A 39-year-old man with HIV, CD4 298, HIV RNA 23,000 cps/ml, never on ART is diagnosed with pulmonary TB. The plan is to start INH, RIF, PZA, and ETH pending susceptibilities. He agrees to start ART and genotype is wild-type.

Which of the following ART regimens do you recommend?

A. TDF/emtricitabine/efavirenz
B. TAF/emtricitabine + atazanavir (boosted)
C. TDF/emtricitabine + atazanavir (unboosted)
D. TAF/emtricitabine + darunavir (boosted)

HIV-TB Co-infection (2)

- Include a rifamycin in the regimen.
  - rifampin
    - significantly ↓ **TAF** – current FDA label: not recommended
    - significantly ↓ ALL **PIs** – do not use
    - ↓ **dolutegravir (DTG)** (need to ↑ DTG to 50 mg bid)
    - significantly ↓ **bictegravir (BIC)** – do not use (conflicting data)
    - ↓ NNRTI concentrations: **efavirenz (EFV)** 600 mg daily is recommended
  - rifabutin: preferred; more manageable drug interactions with protease inhibitors
- For IRIS, continue both ART and TB meds while managing the syndrome.
- Treatment support, including directly observed therapy (DOT) of TB rx is strongly recommended.

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Question #4

A 55-year-old with HIV not previously on rx, CD4 320 and HIV RNA 67,000 cps/ml

Lab testing reveals: toxoplasma Ab+; CMV Ab+; HAV total Ab+; HBV surface Ag+, core Ab+, surface Ab-; HCV Ab-; RPR NR

Of the following, which ART regimen would you recommend?

A. abacavir/lamivudine/dolutegravir
B. dolutegravir/lamivudine
C. tenofovir (TAF or TDF) + atazanavir (boosted)
D. tenofovir (TAF or TDF)/emtricitabine + darunavir (boosted)

HIV-HBV Co-infection

- Some ART has activity against HBV
  - lamivudine (3TC), emtricitabine (FTC), tenofovir (TDF and TAF)
- Some HBV drugs have activity against HIV
  - entecavir (can select M184V) *McMahon NEJM 2007;356:2614*
- If treatment started, treat both optimally
  - 2 active agents for HBV (TAF or TDF) + (3TC or FTC)
  - + 3rd drug for HIV (preferred = BIC or DTG)
  - If tenofovir cannot be used, start a fully suppressive regimen and add entecavir

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HIV-HCV Co-Infection

- Anyone with HCV should be screened for HIV.
- High-risk HIV+ patients should be screened for HCV annually.
- ART should be started in those with concomitant HCV.
  - Same initial regimens recommended, but caution with drug-drug interactions and overlapping toxicities.
- Patients with HIV and HCV should be evaluated for HCV therapy (including assessing liver fibrosis stage).
  - Also evaluate for HBV co-infection.
- HCV direct-acting antiviral regimens → high cure rates

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Question #5

A 26-year-old woman with HIV on abacavir/lamivudine + efavirenz with CD4 630 and VL suppressed below detection becomes pregnant.

What do you recommend regarding ART?

A. Discontinue ART until 2nd trimester.
B. Change abacavir to zidovudine.
C. Change efavirenz to bictegravir.
D. Continue current regimen.

Antiretrovirals in Pregnancy

- ART recommended for all pregnant people, as early as possible, regardless of CD4 or VL level (rx and prevention of MTCT)
  - Perform drug-resistance testing if VL >500-1000 cps/ml
  - Start (or continue if safe/tolerated) standard 3-drug ART as early as possible (while awaiting drug resistance testing):
    - 2-drug regimens can be continued, if virologically suppressed
    - Modify regimen when drug resistance testing results available
  - ART does NOT increase the risk of birth defects
- Near delivery, if HIV RNA >1000 (or unknown), use intravenous zidovudine, and recommend Cesarean section at 38 weeks

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ART in Pregnancy: NRTI

- Preferred:
  - abacavir/lamivudine
  - tenofovir (TAF or TDF)/(emtricitabine or lamivudine)
- Alternative:
  - zidovudine/lamivudine
- IV zidovudine recommended close to delivery if VL >1000

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ART in Pregnancy: NNRTI

- Alternative:
  - efavirenz (birth defects reported in primate studies, NO evidence in human studies and extensive experience; screen for depression)
  - rilpivirine (NOT with baseline VL >100K or CD4 <200 or PPIs)
- Insufficient data: doravirine
- Not recommended (could continue if on):
  - etravirine (not for treatment-naïve pts)
  - nevirapine (toxicity, need for lead-in dosing, low barrier to resistance)

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ART in Pregnancy: PI

- Preferred:
  - darunavir/ritonavir (need to use bid)
- Alternative:
  - atzanavir/ritonavir
- Not recommended:
  - cobicistat (↓ drug concentrations, limited experience)
  - lopinavir/ritonavir (side effects, need to use bid; could continue if on; may need to ↑ dose)

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ART in Pregnancy: INSTI

- Preferred:
  - dolutegravir (neural tube defects not significantly ↑ vs. other ART)
- Alternative:
  - bictegravir
  - raltegravir (need to use bid)
- Not recommended:
  - elvitegravir/cobicistat (↓ drug concentrations)
  - IM cabotegravir + rilpivirine

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ART in Pregnancy: Other

- **Not recommended:**
  - 2-drug regimens (e.g. dolutegravir/lamivudine, dolutegravir/rilpivirine; could continue if on)
  - cobicistat as a booster (for EVG or PIs)
  - enfuvirtide (limited data; could continue if on)
  - fostemsavir (limited data; could continue if on)
  - ibalizumab (limited data; could continue if on)
  - lenacapavir (limited data; could continue if on)
  - maraviroc (need tropism testing; limited data, could continue if on)

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Question #6

A 34-year-old nurse without HIV sustains a needlestick from a patient with HIV who has not taken ART for 2 years.

Which of these post-exposure (PEP) regimens do you recommend?

A. tenofovir (TDF)/emtricitabine
B. tenofovir (TDF)/emtricitabine + integrase inhibitor
C. tenofovir (TAF)/emtricitabine + integrase inhibitor
D. tenofovir (TDF)/emtricitabine + protease inhibitor

Antiretrovirals for PEP (1)

Postexposure prophylaxis (PEP) for occupational exposure:

- Assess nature of exposure:
  source fluid, volume of fluid, type of exposure, timing
- Assess exposure source; HIV and hepatitis testing
- Testing (baseline, 6 + 12 wks + 6 months with standard HIV Ab or 6 wks + 4 months if new HIV Ab/p24 test used) and counseling
- Offer 4 weeks of rx for recognized transmission risk
  - start ASAP (within 72 hours)
  - **tenofovir (TDF)/emtricitabine + dolutegravir** (not in women in early pregnancy or sexually active and not on birth control) or **raltegravir**
  - adjust regimen for possibility of resistance in source patient
  - f/u within 72 hours

PHS Guidelines updated 5/23/18

Antiretrovirals for PEP (2)

PEP for non-occupational exposure:

- Presentation ≤72 hours with substantial risk exposure from HIV+ or likely to be HIV+ – recommended
- Presentation >72 hours or no substantial risk of exposure – not recommended

- Testing: Do rapid HIV (Ag)/Ab test or if results not available, start PEP
- Prior to PEP: BUN/creatinine, LFTs, STI testing (CT, GC, syphilis), HBV/HCV testing, pregnancy testing

- Treatment: 4 weeks of
  - Preferred: **TDF/FTC + [dolutegravir** or **raltegravir]**
  - Alternative: **TDF/FTC + darunavir/ritonavir**

https://www.cdc.gov/hiv/clinicians/prevention/prescribe-pep.html#regimens

Question #7

23 year old man without HIV with a partner with HIV on ART with HIV RNA suppressed below detection asks about starting pre-exposure prophylaxis (PrEP).

In addition to safer sex counseling, which of these do you recommend?

A. Nothing – PrEP is not indicated.
B. PrEP with tenofovir (TDF)/emtricitabine daily.
C. PrEP with tenofovir (TAF)/emtricitabine "on demand".
D. PrEP with bictegravir/tenofovir (TAF)/emtricitabine daily.

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CDC Guidance for PrEP:

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

- Inform all sexually active adults and adolescents about PrEP
- Before starting:
  - exclude acute and chronic HIV infection (by HIV testing and symptoms)
  - assess baseline CrCl, screen for STIs and HBV infection
- Prescribe PrEP for people with ongoing risk from sex or injecting drugs:
  - tenofovir (TDF)/emtricitabine for ♂ and ♀
  - tenofovir (TAF)/emtricitabine for ♂ ONLY
  - IM cabotegravir for ♂ and ♀
  - provide risk reduction, adherence counseling, condoms
- On PrEP:
  - HIV testing every 3-4 months, monitor CrCl every 6 (age >50 or CrCl <90) or 12 months
  - risk reduction, condoms, STI assessments/treatment
  - evaluate the need to continue PrEP

Conclusions

1. Acute (and recent) HIV – ART recommended.
2. Acute OI – ART within 2 weeks of diagnosis reduces mortality; caution with CNS opportunistic infections.
3. TB – Early ART prolongs survival; caution with rifamycin drug interactions.
4. Hepatitis B and C co-infection – Consider antiviral activity, drug-drug interactions, drug toxicities.
5. Pregnancy – Treat and reduce MTCT; modify ART recommendations based on safety and experience.
6. Post-exposure prophylaxis (PEP) – ART within 72 hours; give for 4 weeks; adjust for known drug resistance.
7. Pre-exposure prophylaxis (PrEP) – TDF/FTC (♂+♀), TAF/FTC (♂), IM CAB (♂+♀)

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